ROBUST SUMMARIES and SIDS DOSSIER for:

n-BUTYL PROPIONATE

.....

CAS No. 590-01-2

Sponsor Country: U.S.A.

DATE: December 2005

December 2005

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SIDS PROFILE

DATE: December 2005

1.01 A.	**CAS No.**	590-01-2
1.01 C.	**CHEMICAL NAME (OECD Name)**	n-Butyl Propionate
1.01 D.	**CAS DESCRIPTOR**	Not available.
1.01 G.	**STRUCTURAL FORMULA**	CH3-CH2-COO-CH2-CH2-CH2 -CH3
	OTHER CHEMICAL IDENTITY INFORMATION	Not available.
1.5	**QUANTITY**	2-5 Million Pounds (in N.A.)
1.7	**USE PATTERN**	Automotive and appliance coatings, OEM applications, enamels, lacquers, inks. Also used in polymerisation reaction for acrylic resins. Not consumer applications.
1.9	**SOURCES AND LEVELS OF EXPOSURE**	Internal users: Storage/filling at production facility: Mini plant: Laboratory: Production facility: Maintenance: Disposal:
ISSUES FOR DISCUSSION (IDENTIFY, IF ANY)		

SIDS SUMMARY

DATE: December 2005

590-01-2 n-butyl propionate Study		Info Available Y/N	OECD Study Y/N	GLP Y/N	Other Study Y/N	Estimation Method Y/N	Acceptable Y/N	Testing Required Y/N
PHYSICAL CHEMICAL DATA								
2.1	Melting Point	Y	N	N	Y	N	Y	N
2.2	Boiling Point	Y	N	N	Y	N	Y	N
2.3	Density	Y	N	N	Y	N	Y	N
2.4	Vapor Pressure	Y	N	N	Y	N	Y	N
2.5	Partition Coefficient	Y	N	N	Y	N	Y	N
2.6.	Water Solubility	Y	N	N	Y	N	Y	N
	pH and PkA values	N			N	N		N
2.12	Oxidation Reduction Potential	N			N	N		N
ENVIRONMENTAL FATE and PATHWAYS								
3.1.1	Photodegradation	Y	N	N	N	Y	Y	N
3.1.2	Stability in water	Y	N	N	N	Y	Y	N
3.2	Monitoring data	N						N
3.3	Transport and Distribution	Y	N	N	N	Y	Y	N
3.5	Biodegradation	Y	N	N	N	N	Y	N
	OTHER ENVIR FATE STUDIES RECEIVED							
	ECOTOXICITY							
4.1	Acute Toxicity to Fish	Y	Y	Y	Y	N	Y	N
4.2	Acute Toxicity to Daphnia	Y	Y	Y	Y	N	Y	N
4.3	Toxicity to Algae	Y	y	y	N	N	Y	N
4.5.2	Chronic Toxicity to Daphnia	N						N
4.6.1	Toxicity to Soil Dwelling Organisms	N						N
4.6.2	Toxicity to Terrestrial Plants	N						N
4.6.3	Toxicity to Birds	N						N
	OTHER ECOTOXICITY STUDIES RECEIVED							

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SIDS SUMMARY (Continued)

590-01-2 n-butyl propionate Study		Info Available Y/N	OECD Study Y/N	GLP Y/N	Other Study Y/N	Estimation Method Y/N	Acceptable Y/N	Testing Required Y/N
TOXICITY								
5.1.1	Acute Oral	Y	N	N	Y	N	Y	N
5.1.2	Acute Inhalation	Y	Y	N	Y	N	Y	N
5.1.3	Acute Dermal	Y	Y	N	Y	N	Y	N
5.4	Repeated Dose	Y	N	Y	Y	N	Y	N
5.5	Genetic Toxicity *in vitro*	Y						
	-Gene Mutation	Y	N	Y	Y	N	Y	N
5.6	-Chromosomal Aberration	Y	Y	Y	N	N	Y	N
	Genetic Toxicity *in vivo*	Y						
5.8	-Chromosome Aberration	Y	N	Y	Y	N	Y	N
5.9	Reproduction Toxicity	Y	N	Y	Y	N	Y	N
5.11	Development/Teratogenicity	Y	N	N	Y	N	Y	N
	Human Experience							
OTHER TOXICITY STUDIES RECEIVED								

1.0 GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

A.	**CAS-Number**	590-01-2
B.	**Name** *(IUPAC name)*	Propionic acid, n-butyl ester
C.	**Name** *(OECD name)*	n-Butyl Propionate
D.	**CAS Descriptor**	
E.	**EINECS-Number**	
F.	**Molecular Formula**	C7 H14 O2
G.	**Structural Formula**	CH3-CH2-COO-CH2-CH2-CH2-CH3
H.	**Substance Group**	Not applicable
I.	**Substance Remark**	
J.	**Molecular Weight**	130.19

1.02 OECD INFORMATION

A. **Sponsor Country:** U.S.A.

B. **Lead Organisation:**

Name of Lead Organisation: American Chemistry Council
Contact person: W. D. (Doug) Anderson
Address: 1300 Wilson Blvd.
Arlington, VA 22209
U.S.A.
Tel: 703-741-5000
Fax: 703-741-6000

1.1 GENERAL SUBSTANCE INFORMATION

A. **Type of Substance** element [ ]; inorganic [ ]; natural substance [ ]; organic [X]; organometalic [ ]; petroleum product [ ]

B. **Physical State** *(at 20°C and 1.013 hPa)*
gaseous [ ]; liquid [X]; solid [ ]

C. **Purity** *(indicate the percentage by weight/weight)*

>99% weight/weight

1.2 SYNONYMS

propionic acid, n-butyl ester
propanoic acid, n-butyl ester
propionic acid butyl ester
propanoic acid butyl ester
n-butyl propionate
butyl propionate
UCAR™ n-butyl propionate

1.3 IMPURITIES

CAS No:	71-36-3
EINECS No:	
Name:	n-butanol
Value:	<0.5%
Remarks:	
Reference:	Union Carbide Corporation. Material Safety Data Sheet# 837: UCAR™ n-Butyl Propionate. Effective date 06/07/2001. Union Carbide Chemicals and Plastics Technology Corporation, The Dow Chemical Company, Danbury, CT.

CAS No:	79-09-4
EINECS No:	
Name:	propanoic acid
Value:	<0.01%
Remarks:	
Reference:	Union Carbide Corporation. Material Safety Data Sheet# 837: UCAR™ n-Butyl Propionate. Effective date 06/07/2001. Union Carbide Chemicals and Plastics Technology Corporation, The Dow Chemical Company, Danbury, CT.

1.4 ADDITIVES

CAS No:	None
EINECS No:	
Name:	
Value:	
Remarks:	Inhibitors and stabilisers are not applicable. n-Butyl propionate is stable and hazardous polymerization will not occur.
Reference:	Union Carbide Corporation. Material Safety Data Sheet# 837: UCAR™ n-Butyl Propionate. Effective date 06/07/2001. Union Carbide Chemicals and Plastics Technology Corporation, The Dow Chemical Company, Danbury, CT.

1.5 QUANTITY

	2-5 million pounds
Remarks:	production in North America in 2001.
Reference:	The Dow Chemical Company.

1.6 LABELLING AND CLASSIFICATION

Labelling

Type:	
Specific limits:	
Symbols:	
Note:	
R-phrases:	R-10 flammable
S-phrases:	S-2, S-23
Text of S-phrases:	S-2: Keep out of reach of children S-23: Do not breathe gas, fumes, vapour or spray
Remarks:	

Classification

Type:	
Category of danger:	
R-phrases:	
Remarks:	

1.7 USE PATTERN

A. General

Type of Use:	**Category: Non dispersive**
	Use resulting in inclusion into or onto matrix
Type of Use:	**Category: Wide dispersive**
industrial	Basic industry: basic chemicals
industrial	Chemical industry: process solvent applications
industrial	Chemical industry: solvent for adhesives
industrial	Chemical industry: solvent for printing inks and coatings
industrial	Chemical industry: solvent for nitrocellulose
use	Manufacture of adhesives, inks, coatings, and cleaning fluids
use	Retardant in lacquer thinner

Reference:

Glancy, C.W. 1988. New solvents for high solids coatings. Mod. Paint. Coatings 78: 35-44

Sullivan, D.A. 1995. Solvent selection in today's regulatory environment. Mod. Paint. Coatings 85: 38-42.

Lewis, R.L., Sr. 1993. Hawley's Condensed Chemical Dictionary, 12th ed. New York: Van Nostrand Reinhold

Remark:	Butyl propionate is used for high solids coating in automotive refinishes, OEM applications, and appliance coatings. It is also used in the manufacture of cleaning fluids, enamels, lacquers, and printing inks. Butyl propionate is also used in polymerisation reactions for acrylic resins. Butyl propionate is not used in consumer applications.
Reference:	The Dow Chemical Company.

B. Uses in Consumer Products

Not used in consumer applications.

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Type of Limit:	TWA (US)
Value:	
Short Term Exposure Limit Value:	
Time Schedule:	
Remark:	None

Type of Limit other:	OSHA PEL (US)
Value:	
Short Term Exposure Limit Value:	
Time Schedule:	
Remark:	None

Type of Limit:	NIOSH REL (US)
Value:	
Short Term Exposure Limit Value:	
Time Schedule:	
Remark:	None

1.9 SOURCES OF EXPOSURE

Remark: Use as a solvent may lead to its release into the environment. Occurs naturally in fruits and may be released as a plant volatile. The general population may be exposed to very low butyl propionate through consumption of food products. Occupational exposure may occur through inhalation or dermal contact with this compound at workplaces where butyl propionante is produced or used as a solvent.

1.10 ADDITIONAL REMARKS

Remark: NFPA Hazard Classifications:
Flammability: 3 (easily ignited under almost all normal conditions)

Reactivity: 0 (normally stable even under fire exposure conditions)
Health: 2 (material hazardous to health-exposure would cause irritation with significant residual injury)

Reference: NFPA. 2002. National Fire Protection Association. Fire Protection Guide to Hazardous Materials, 13th edition. NFPA. Quincy, MA.

Remark: Disposal: n-butyl propionate is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration.

Reference: Union Carbide Corporation. Material Safety Data Sheet# 837: UCAR™ n-Butyl Propionate. Effective date 06/07/2001. Union Carbide Chemicals and Plastics Technology Corporation, The Dow Chemical Company, Danbury, CT.

Remark: USDOT/UN/NA/IMO number: 1914
IMO
Standard transportation number:
class: 3
label: 3
pack. gr.: PGIII
Marine pollutant:
Label: Flammable liquid
Proper shipping name: Butyl Propionate

Reference: Union Carbide Corporation. Material Safety Data Sheet# 837: UCAR™ n-Butyl Propionate. Effective date 06/07/2001. Union Carbide Chemicals and Plastics Technology Corporation, The Dow Chemical Company, Danbury, CT.

2.0 PHYSICAL-CHEMICAL DATA

2.1 MELTING POINT

(a)	Preferred result	reliability score = 2, valid with restrictions; data from handbook or collection of data
	Value:	-89 degree C
	Remark :	-128.2 degree F
	Reference:	Sax, I.N. and Lewis, R.J., Sr. (eds). Hawley's Condensed Chemical Dictionary, 11th Edition. New York, NY: Van Nostrand Reinhold Company, 1987. 74. Budavari, S.B. (ed.). 1996. The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals, 12th Edition. Whitehouse Station, NJ: Merck & Co., Inc.
(b)	Value:	-89.5 degree C
	Remark:	129.1 degree F
	Reliability:	score = 2, valid with restrictions; data from handbook or collection of data
	Reference:	Lide, D.R. (ed) CRC Handbook of Chemistry and Physics, 76th ed. Boca Raton, FL: CRC Press Inc., 1995-1996.

2.2 BOILING POINT

(a)	Preferred result	reliability score = 2, valid with restrictions; data from handbook or collection of data
	Value:	146.8 degree C
	Remark:	296.2 degree F
	Reference:	Budavari, S.B. (ed.). 1996. The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals, 12th Edition. Whitehouse Station, NJ: Merck & Co., Inc.
(b)	Value:	146 degree C
	Remark:	294.8 degree F
	Reliability:	score = 2, data from handbook or collection of data
	Reference:	Sax, I.N. and Lewis, R.J., Sr. (eds). Hawley's Condensed Chemical Dictionary, 11th Edition. New York, NY: Van Nostrand Reinhold Company, 1987.
(c)	Value:	146 degree C
	Remark:	Reported as 295 degree F
	Reliability:	score = 2, valid with restrictions; data from handbook or collection of data
	Reference:	NFPA. 1986. National Fire Protection Association. Fire Protection Guide to Hazardous Materials. 9th edition. NFPA. Quincy, MA.
(e)	Value:	132.1 degree C
	Remark:	269.8 degree F
	Reference:	Lide, D.R. (ed) CRC Handbook of Chemistry and Physics, 76th ed. Boca Raton, FL: CRC Press Inc., 1995-1996.

2.3 DENSITY

(a)	Preferred result	reliability score = 2, valid with restrictions; data from handbook or collection of data
	Value:	0.8754 g/cm3
	Temperature:	20 degree C
	Method:	
	Year:	
	GLP:	
	Reference:	Budavari, S.B. (ed.). 1996. The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals, 12th Edition. Whitehouse Station, NJ: Merck & Co., Inc.
(b)	Value:	0.875 g/cm3
	Temperature:	20 degree C

	Method other:	
	Year:	
	GLP:	
	Reliability:	score = 2, valid with restrictions; data from handbook or collection of data.
	Reference:	Sax, I.N. and Lewis, R.J., Sr. (eds). Hawley's Condensed Chemical Dictionary, 11th Edition. New York, NY: Van Nostrand Reinhold Company, 1987. 74. Lide, D.R. (ed) CRC Handbook of Chemistry and Physics, 76th ed. Boca Raton, FL: CRC Press Inc., 1995-1996.
(d)	Value:	0.874 g/cm3
	Temperature:	15.5 degree C
	GLP:	
	Reliability:	score = 2, valid with restrictions, data from handbook or collection of data.
	Reference:	Sax, I.N. and Lewis, R.J., Sr. (eds). Hawley's Condensed Chemical Dictionary, 11th Edition. New York, NY: Van Nostrand Reinhold Company, 1987. 74.
(e)	Value:	0.9
	Remark:	relative density (water = 1.0)
	Reliability:	score = 2, valid with restrictions; data from handbook or collection of data.
	Reference:	NFPA. 2002. National Fire Protection Association. Fire Protection Guide to Hazardous Materials. 13th Edition. NFPA. Quincy, MA.

2.4 VAPOUR PRESSURE

(a)	Preferred result	reliability score = 2, valid with restrictions; data from handbook or collection of data
	Value:	3.8 hPa
	Temperature:	20 degree C
	Remark:	Reported as 0.38 kPa or 2.86 mm Hg
	Reference:	International Programme on Chemical Safety. Chemical data sheet for Butyl Propionate (CAS 590-01-2). ICSC 0556, dated November 1998.
(b)	Value:	3.8 hPa
	Temperature:	25 degree C
	Remark:	Reported as 4.4 mm Hg at 25°C
	Reliability:	score = 2, valid with restriction; accepted calculation method.
	Reference:	U.S.Environmental Protection Agency. 2003. Experimental water solubility and vapor pressure values reported by EPISuite software, version 3.11. U.S. Environmental Protection Agency;

available at
ttp://www.epa.gov\oppt\expousre\docs\episuitedl.htm.

2.5 PARTITION COEFFICIENT $log_{10}P_{ow}$

(a)	Preferred result	reliability score = 2; valid with restriction, accepted calculation method
	$log\ P_{ow}$	2.34
	Method:	calculated using KOWWIN (v. 1.66), using the molecular structure fragment method.
	Year:	2000
	Reference:	KOWWIN v. 1.66. 2000. EPIWIN (Estimation Program for Windows) Version 3.10. U.S. Environmental Protection Agency.
(b)	$log\ P_{oct}$:	2.025
	Method:	calculated
	Year:	
	Remark:	$log\ P_{oct}$ calculated using the regression equation $log\ P_{oct} = 4.5 - 0.75\ log\ S$, where S is the solubility of butyl propionate (2000 mg/l)
	Reliability:	score = 2, valid with restriction; data from handbook or collection of data
	Reference:	Verschueren, K. 2001. Handbook of Environmental Data on Organic Chemicals, 4th Edition. New York, NY: John Wiley & Sons, Inc.

2.6 WATER SOLUBILITY

(a)	Preferred result	score = 2, valid with restriction, accepted calculation method
	Value:	1428 mg/L
	Method:	calculated using WSKOWWIN (v. 1.40), using a regression equation with log Kow = 2.34 and melting point = -89°C
	Year:	2000
	Reference:	WSKOWWIN v. 1.40. 2000. EPIWIN (Estimation Program for Windows) Version 3.10. U.S. Environmental Protection Agency.
(b)	Value:	1500 mg/L
	Temperature:	25 degree C
	Reliability:	score = 2, valid with restriction; accepted calculation method.
	Reference:	U.S.Environmental Protection Agency. 2003. Experimental water solubility and vapor pressure values reported by EPISuite software, version 3.11. U.S. Environmental Protection Agency; available at ttp://www.epa.gov\oppt\expousre\docs\episuitedl.htm
(c)	Value:	2000 mg/l at 20 degree C
	Description:	slightly soluble

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	Remark:	Reported as 0.2% at 20 degree C
	Reliability:	score = 4, not assignable; insufficient data for assessment.
	Reference:	Union Carbide Corporation. Material Safety Data Sheet # 837: UCAR™ n-Butyl Propionate. Effective date 06/07/2001.

2.7 FLASH POINT *(liquids)*

(a)	Preferred result	reliability score = 1, meets national standard (ASTM) methods
	Value:	38 degree C
	Type:	Setaflash closed cup
	Method:	ASTM D3828
	Remark:	100 degree F
	Reference:	Union Carbide Corporation. Material Safety Data Sheet # 837: UCAR™ n-Butyl Propionate. Effective date 06/07/2001. Union Carbide Chemicals and Plastics Technology Corporation, The Dow Chemical Company, Danbury, CT.
(b)	Value:	32.2 degree C
	Type:	no data
	Remark:	90 degree F
	Reliability:	score = 2, valid with restrictions; data from handbook or collection of data.
	Reference:	Sax, I.N. and Lewis, R.J., Sr. (eds). Hawley's Condensed Chemical Dictionary, 11th Edition. New York, NY: Van Nostrand Reinhold Company, 1987. 74.
(c)	Value:	32 degree C
	Type:	closed cup
	Remark:	90 degree F
	Reliability:	score = 2, valid with restrictions; data from handbook or collection of data.
	Reference:	NFPA. 2002. National Fire Protection Association. Fire Protection Guide to Hazardous Materials, 13th edition. NFPA. Quincy, MA.

2.8 AUTO FLAMMABILITY *(solid/gases)*

(a)	Preferred result	reliability score = 2; valid with restrictions; data from handbook or collection of data
	Value:	426.1 degree C
	Remark:	autoignition temperature; reported as 799 degree F
	Reference:	NFPA. 2002. National Fire Protection Association. Fire Protection Guide to Hazardous Materials, 13th edition. NFPA. Quincy, MA.
(b)	Value:	426.7 degree C
	Remark:	autoignition temperature; reported as 800 degree F

	Reliability:	score = 2, valid with restrictions; data from handbook or collection of data.
	Reference:	Sax, I.N. and Lewis, R.J., Sr. (eds). Hawley's Condensed Chemical Dictionary, 11th Edition. New York, NY: Van Nostrand Reinhold Company, 1987. 74.

2.9 FLAMMABILITY

(a)	Preferred result	reliability score = 4, data insufficient for assessment
	Value:	Flammable range 1.19 – 7.57 vol % (11,900 – 75,700 ppm)
	Remark:	n-butyl propionate, >99.5%
	Reference:	Union Carbide Corporation. Material Safety Data Sheet # 837: UCAR™ n-Butyl Propionate. Effective date 06/07/2001.

2.10 EXPLOSIVE PROPERTIES

Remark:	Flammability hazard rating: 3. Flammable liquid, vapors may form explosive mixtures with air; containers may explode when overheated. Class IC flammable liquid; easily ignited under almost all normal temperature conditions. Water may be ineffective in controlling or extinguishing fires.
Reliability:	score = 2, valid with restrictions; data from handbook or collection of data.
Reference:	NFPA. 2002. National Fire Protection Association. Fire Protection Guide to Hazardous Materials, 13th edition. NFPA. Quincy, MA.

2.11 OXIDIZING PROPERTIES

Remark:	Not an oxidizer. Incompatible with strong oxidizers.
Reference:	Union Carbide Corporation. Material Safety Data Sheet # 837: UCAR™ n-Butyl Propionate. Effective date 06/07/2001.

2.12 ADDITIONAL REMARKS

Remark:	Very soluble in ethanol and ether.
Reliability:	score = 2, valid with restrictions; data from handbook or collection of data.
Reference:	Lide, D.R. (ed). 1995. CRC Handbook of Chemistry and Physics, 76th ed. Boca Raton, FL: CRC Press Inc. Budavari, S.B. (ed.). 1996. The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals, 12th Edition. Whitehouse Station, NJ: Merck & Co., Inc.
Remark:	Miscible with all coal tar and petroleum distillates, soluble in alcohol and ether, very slightly soluble in water. Weight per gallon: 7.3 lb.
Reliability:	score = 2, valid with restrictions; data from handbook or collection of data.
Reference:	Sax, I.N. and Lewis, R.J., Sr. (eds). Hawley's Condensed Chemical Dictionary, 11th Edition. New York, NY: Van Nostrand Reinhold Company, 1987. 74.

2.13 ADDITIONAL DATA

Remark:	Vapor density: 4.5 (air = 1) Evaporation rate: 0.45 (butyl acetate =1)

Reliability: score = 2, valid with restrictions; data from handbook or collection of data.
Reference: NFPA. 2002. National Fire Protection Association. Fire Protection Guide to Hazardous Materials. 13th edition. NFPA. Quincy, MA.

Remark: Lower explosion limit (LEL): 1.19 vol % (11,900 ppm)
Upper explosion limit (UEL): 7.57 vol % (75,700 ppm)
Reliability: score = 4, data insufficient for assessment
Reference: Union Carbide Corporation. Material Safety Data Sheet # 837: UCAR™ n-Butyl Propionate. Effective date 06/07/2001. Union Carbide Chemicals and Plastics Technology Corporation, The Dow Chemical Company, Danbury, CT.

3.0 ENVIRONMENTAL FATE AND PATHWAYS

3.1 STABILITY

3.1.1 PHOTODEGRADATION

(a) Preferred value (score = 2), valid with restriction; accepted calculation method

Deleted:

Light source:	
Light spectrum:	
Relative intensity:	based on intensity of sunlight
Degradation:	51.1 hours
Method:	estimated using AOPWIN, version 1.90
Year:	2000.
GLP:	not applicable, calculated value
Test substance:	n-butyl propionate
Remark :	Atmospheric photo-oxidation potential was estimated using the submodel AOPWIN (v. 1.90) that calculates a second order half-life with units of cm^3/molecules-cm. Vapor-phase n-butyl proprionate is expected to degrade in the atmosphere by reaction with photochemically produced hydroxyl (OH) radicals. Chemical-specific input parameters for EPIWIN modelling were: molecular weight: 130.19 g/mol; vapor pressure: 2.86 mm Hg; Log kow: 2.34 (calculated by EPIWIN); Melting point: -89°C; Water solubility: 1428 mg/L (calculated by EPIWIN). The 2nd order rate constant was calculated as 5.024×10^{-12} cm^3/molecule*sec at 25°C. Based on the presence of 1.5×10^6 OH molecules/cm^3, and assuming 12 hours of sunlight per day, the estimated half-life of n-butyl propionate is 2.129 days or 51.096 hours.
Reference:	AOPWIN Version 1.90. 2000. Atmospheric Oxidation Program for Windows. EPIWIN (Estimation Program Interface for Windows) Version 3.10. U.S. Environmental Protection Agency.

3.1.2 STABILITY IN WATER

(a)	Preferred result:	score = 1, reliable without restriction, GLP guideline study
	Test substance:	n-butyl propionate, purity 99.92%
	Type:	abiotic hydrolysis
	Method:	OECD Guideline 111: Hydrolysis as a Function of pH, 1981. EEC Commission Directive 87/302/EEC
	Year:	1981
	GLP:	yes
	t1/2 at pH 4:	174 days
	t1/2 at pH 7:	131 days
	t1/2 at pH 9:	13.2 days
	Remark:	The hydrolysis kinetics of n-butyl propionate was evaluated at 50, 60, and 70 °C in 0.05 M buffered solutions at pH 4, 7, and 9. The buffered solutions were prepared with potassium biphthalate, potassium phosphate, and sodium borate, respectively. All test solutions were incubated in the dark to minimize possible photochemical reactions. All solutions and equipment were sterilized to reduce the potential for biodegradation of the test material. Sample concentrations were determined using a gas chromatograph equipped with a flam ionisation detector. Selected test solutions were assayed for microbial contamination at the conclusion of Tier II testing; no growth was observed on agar plates inoculated with test solutions after a 5-day incubation interval. Due to limited solubility of the test material, stock solutions of approximately 20,000 mg/L were prepared in acetonitrile. A 1.2 ml aliquot of the stock solution was added to respective 250 ml of sterile buffer solution, for a nominal concentration of approximately 100 mg/L. A preliminary test (Tier I probe) was conducted at 50 °C at pH 4, 7, and 9 to determine the susceptibility of the test material to hydrolysis. Each buffered solution was dosed with 100 mg/L test material as described above. Hydrolysis of butyl propionate reached 20.7, 18.6, and 32.4% after 2.3 days at pH 4, 7, and 9, respectively. After 5 days, hydrolysis of butyl propionate was 26.6, 27,6, and 100% at pH 4, 7, and 9, respectively. This translated into half-lives of 24.9, 21.7, and 0.8 days, at pH 4, 7, and 9, respectively. Because more than 10% hydrolysis was observed after 5 days, and the half life was greater than 2.4 hours at 50 °C, more extensive kinetic evaluations were required to comply with test guidelines. Tier II evaluations were conducted in pH 4, 7, and 9 buffers at 50, 60, and 70 °C. Buffered test solutions were dosed with 100 mg/L of the test material at each pH and temperature. Hydrolysis rates for n-butyl propionate increased with temperature and followed pseudo-first order kinetics. Half lives at 50, 60, and 70 °C were determined to be 35.3, 19.2, and 11.6 days at pH 4;

	20.1, 12.5, and 5.7 days at pH 7; and 0.92, 0.27, and 0.14 days at pH 9. Using the Arrhenius relationship (logarithm of pseudo-first order rate constant vs. reciprocal of temperature in °K), the predicted hydrolysis half-life at 25 °C in pH 4, 7, and 9 buffered solutions are 174, 131, and 13.2 days, respectively.
Reference:	Davis, J.W. and Marty, G.T. 2004. n-Butyl Propionate: Evaluation of Hydrolysis as a Function of pH Using OECD Guideline 111 (unpublished study). Toxicology & Environmental Research and Consulting, Study ID 031068. The Dow Chemical Company, Midland, MI.

3.1.3 STABILITY IN SOIL

No data available

3.2 MONITORING DATA (ENVIRONMENT)

(a) Type of Measurement
Media:
Remark: No data available
Reference:

3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

(a)	Type:	volatilisation from surface waters
	Test substance:	n-butyl propionate
	Method:	calculated using EPISUITE v. 3.10
	GLP:	not applicable, calculated value
	Result:	half-life from a model river: 2.487 hours Half-life from a model lake: 5.117 days
	Remark:	Based on Henry's law constant of 3.431 x 10-4 atm-m3/mol, vapor pressure of 2.86 mm Hg, water solubility of 1428 mg/L, and molecular weight of 130.19 g/mol. , Model defaults used were for a model river: 1 m deep water flow at 1 m/sec, wind speed of 5 m/sec; for a model lake: 1 m deep, water flow 0.05 m/sec, wind spped 0.5 m/sec.
	Reliability:	score = 2, valid with restriction; accepted calculation method.
	Reference:	EPISUITE v. 3.10. 2000. U.S. Environmental Protection Agency.
(b)	Type:	Soil or sediment partition coefficient (Koc)
	Test substance:	n-butyl propionate

	Method:	Calculated using EPISUITE v. 3.10 and PCKOCWIN v. 1.66 using structural features of the molecule.
	Result:	Koc = 40.3 L/kg
	GLP:	not applicable, calculated value
	Reliability:	score = 2, valid with restriction; accepted calculation method.
	Reference:	EPISUITE v. 3.10. 2000. U.S. Environmental Protection Agency.
(c)	Type:	Henry's Law constant
	Test substance:	n-butyl propionate
	Method:	Calculated using water solubility of 1428 mg/L, vapor pressure of 2.86 mm Hg, and molecular weight of 130.19 g/mol.
	Result:	3.431×10^{-4} atm-m^3/mol at 25°C
	GLP:	not applicable, calculated value
	Reliability:	score = 2, valid with restriction; accepted calculation method.
	Reference:	EPISUITE v. 3.10. 2000. U.S. Environmental Protection Agency.

3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

(a) Preferred value

Type:	Level III Fugacity-based distribution modelling
Test substance:	n-butyl propionate
Remark:	Default values were assumed for environmental compartment descriptions, dimensions, and properties, advective and dispersive properties. Chemical-specific input parameters were: molecular weight: 130.19 g/mol; vapor pressure: 2.86 mm Hg; Log Kow: 2.34 (calculated by EPIWIN); melting point: -89°C; water solubility: 1428 mg/L (calculated by EPIWIN);. air half-life 51.1 hours; aater and soil half-lives 208 hours, sediment half life, 832 hours. Emissions were assumed to be equal to air, water and soil.
Distribution:	Air: 13.4% Water: 36.7% Soil: 49.8% Sediment: 0.125%
GLP:	not applicable, calculated value
Reliability:	score = 2, valid with restriction; accepted calculation method.
Reference:	EPISUITE v. 3.10. 2000. U.S. Environmental Protection Agency.

Deleted: (b) . Media other: . . air - suspended atmospheric particles¶
Method other: estimate¶
Year:¶
Remark: . According to a model of gas/particle partitioning of semi-volatile organic materials in the atmosphere, butyl propionate is expected to exist solely as a vapour in the ambient atmosphere, based on a vapour pressure of 3.44 mm Hg at 20 degree C.¶
Reliability: score = 2, valid with restrictions; accepted calculation method.¶
Reference: Daubert, T.E. and Danner, R.P. 1989. Physical and Thermodynamic Properties of Pure Chemicals: Data Compilation. New York, NY: Hemisphere Publishing Corp. ¶

3.4 IDENTIFICATION OF MAIN MODE OF DEGRADABILITY IN ACTUAL USE

3.5 BIODEGRADATION

(a)	Preferred study	reliability score = 2, valid with restrictions
	Type:	aerobic
	Inoculum:	settled domestic wastewater
	Concentration:	3, 7, and 10 mg/l
	Contact time:	20 days
	Degradation:	92% after 20 days
	Results:	readily biodegradable
	Kinetic:	5 days = 59% 10 days = 79% 15 days = 84% 20 days = 92%
	Method other:	APHA. 1985. Standard Methods for the Examination of Water and Wastewater, 16th Edition, American Public Health Association, Washington, DC. With modifications described in Price, K.S., Waggy, G.T., and Conway, R.A. 1974. Brine shrimp bioassay and seawater BOD of petrochemicals. J. Water Poll. Control Fed. 46: 63-77
	GLP:	no
	Test substance:	n-butyl propionate, purity not specified
	Remark:	Settled domestic wastewater was filtered through glass wool and then added (3 ml/bottle) as seed material to clean BOD bottles. The bottles were filled with aerated water containing minerals and buffer. Small aliquots of n-butyl propionate were added from a stock solution to yield concentrations of 3.0, 7.0, and 10 mg/l. Dissolved oxygen (DO) was monitored 5 times over the 20 day test interval using a commercial DO meter. Seeded blanks were analysed at each 5-day interval. Additional tests were conducted concurrently with glucose standards to assess toxicity of the test material on the inoculum. Biodegradation values are based on calculated theoretical oxidation (ThOD) of butyl propionate to its lowest energy state (i.e. CO2 and H2O). Results suggest that n-butyl propionate is readily degraded.
	Reference:	Waggy, G.T. 1989. Ecological Fate and Effects Testing of UCC Products and Wastewaters During 1988 (unpublished report). File No. 37073. Project report dated June 27, 1989. Union Carbide Corporation, South Charleston, WV.

3.6 BOD_5,COD OR RATIO BOD_5/COD

BOD_5

(a)	Method other:	APHA. 1985. Standard Methods for the Examination of Water and Wastewater, 16th Edition, American Public Health Association (APHA), Washington, DC.
	BOD_5	59% of ThOD
	GLP:	no

Remark:	BOD_{10} = 79% of ThOD BOD_{20} = 92% of ThOD Biodegradation values are based on calculated theoretical oxidation (ThOD) of butyl propionate to its lowest energy state (i.e. CO2 and H2O).
Reliability:	score = 2; valid with restrictions
Reference:	Waggy, G.T. 1989. Ecological Fate and Effects Testing of UCC Products and Wastewaters During 1988 (unpublished report). File No. 37073. Project report dated June 27, 1989. Union Carbide Corporation, South Charleston, WV.

COD

(a)	Type:	measured
	Method other:	APHA. 1985. Standard Methods for the Examination of Water and Wastewater, 16th Edition, American Public Health Association (APHA), Washington, DC.
	COD:	2.22 mg O_2/mg butyl propionate
	GLP:	no
	Reference:	Waggy, G.T. 1989. Ecological Fate and Effects Testing of UCC Products and Wastewaters During 1988 (unpublished report). File No. 37073. Project report dated June 27, 1989. Union Carbide Corporation, South Charleston, WV.

Ratio BOD_5/COD:

BOD5/COD:	
Remark:	
Reference:	

ThOD

Method other:	calculated by EPISuite v. 3.11
ThOD:	2.34 mg O_2/mg butyl propionate
GLP:	not applicable, calculated value
Reliability:	score = 2, valid with restriction, accepted calculation method
Reference:	U.S. Environmental Protection Agency. 2003. Experimental values reported by EPISuite software, version 3.11. United States Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, D.C.

Deleted:

3.7 BIOACCUMULATION

BCF: 12.59 L/kg

Method other:	Calculated using EPISUITE v.3.10 and BCFWIN v. 2.14 using a log Kow of 2.34 and a regression equation (log BCF = 0.77 Log Kow- 0.70).
Year:	2000
GLP:	not applicable, calculated value
Reliability:	score = 2, valid with restriction, accepted calculation method
Reference:	EPISUITE v. 3.10. 2000. U.S. Environmental Protection Agency.

3.8 ADDITIONAL REMARKS

Remark:	Henry's Constant (H) = 1.237 x 10E-2, calculated using a regression equation; using a vapor pressure of 3.44 mm Hg at 20 degree C and a water solubility of 2000 mg/l at 20 degree C.
Reliability:	score = 2, valid with restrictions; accepted calculation method.
Reference:	Verschueren, K. 2001. Handbook of Environmental Data on Organic Chemicals, 4th Edition. New York, NY: John Wiley & Sons, Inc.

4.0 ECOTOXICOLOGICAL DATA

4.1 ACUTE/PROLONGED TOXICITY TO FISH

(a) preferred result: reliability = 1, valid without restriction. GLP guideline study

Type:	flow-through
Test:	LC50
Species:	*Oncorhynchus mykiss* Walbaum, freshwater rainbow trout
Unit:	mg/L
Exposure Period:	96 hours
LC50:	6.89
NOEC:	1.30
Test substance:	n-butyl propionate, purity 99.7%
Analyt Monitoring.:	yes
Year:	1992
GLP:	yes
Methods:	OECD Guideline for Testing of Chemicals No.203, Fish Acute Toxicity Test, adopted 7/17/92 Directive 92/69/EEC, C.1 Acute Toxicity for Fish, Vol. 35, 12/29/92 U.S. EPA. Toxic Substances Control Act Test Guidelines. 40 CFR 797.1400. Fish Acute Toxicity Test, 07/01/1992. Rainbow trout *Oncorhynchus mykiss* Waldbaum were obtained as juveniles from Thomas Fish Company, Anderson, CA. Juvenile fish were visually inspected on arrival and placed in a holding tank. All fish were maintained on a 16-hour light/8-hour dark transitional photoperiod and observed for more than 14 days prior to testing. During the observational interval, fish were fed a standard aquatic diet (Harlan-Teklad, Madison, WI) at

least once daily. Fish were acclimated to 13.0 + 1 °C for more than 14ays and held without food for at least 48 hours prior to testing.

Laboratory water was obtained from the upper Saginaw Bay of Lake Huron; before use, water is sand-filtered, pH-adjusted with carbon dioxide, carbon-filtered, and UV-irradiated. Alkalinity, conductivity, pH, and hardness were monitored weekly. Water quality criteria in control/dilution water used during the test were as follows (day 0 – day 4):

Hardness (mg $CaCO_3$/L):	62 - 74
Alkalinity (mg $CaCO_3$/L):	23 - 24
Conductivity (μmho/cm):	172 - 175
Residual chlorine:	<10 ppb

Fish averaging 4.4 + 0.3 cm and weighing 0.731 + 0.134 gm were used as test organisms. Definitive testing was conducted in test aquaria constructed of double-strength glass with an approximate volume of 3.7 L.

An intermittent-flow proportional diluter system (Microlab® 500 Precision Dosing System, Hamilton Company, Reno, NV) was used to maintain constant exposure concentrations during the 4-day study interval. The system was designed to deliver up to six test concentrations, vehicle control, and a water control. The diluter was calibrated so that the concentration of the test substance in each treatment below the high concentration was approximately 60% of that in the next higher treatment level. When the duluter cycled, the test substance was blended and flowed into mixting/splitting chambers. During each cycle of the diluter, a volume of 0.060 ml butyl propionate was injected into 5.27 L of laboratory water which resulted in a nominal target concentration of 10 mg/L; subsequent lower nominal test concentrations were 5.91, 3.50, 2.19, 1.33, and 0.653 mg/L butyl propionate, and a water control. Silicone delivery tubes provided approximately 1L test solution to each of two replicate test aquaria for each test dose. The diluter was calibrated prior to test initiation and delivered an average of 7.1 volume turnovers in test aquaria for concentration for each 24-hour interval during the study.

Test aquaria and diluter were positioned in a temperature-controlled water trough and provided a 16-hr light/8-hr dark transitional photoperiod during testing. Temperature, pH, and dissolved oxygen were monitored throughout the 96-hour exposure interval and recorded for each vessel at 0, 24, 48, 72, and 96 hours. Ten fish 60, (two replicates of 5 fish each) were exposed to each nominal concentration. Fish were not fed during

the test. Fish were observed for mortality, and physical and behavioral effects throughout the exposure interval. Dead fish were removed when observed. Terminal body weights and total length measurements were recorded; surviving fish were euthanized with tricaine methanesulfonate prior to taking measurements. The mean terminal body weight of all surviving fish was used to calculate the instantaneous loading rate and the loading rate based on the total solution flow in a 24-hour interval. The loading rate of the test vessels did not exceed 1.0 gm fish per liter of test solution. The average instantaneous loading rate was 1.0 per g fish/L of test solution. The average loading rate based on total solution flow in a 24-hour interval was 0.08 per g fish/L/day.

Butyl propionate test concentrations were selected based on range-finding tests using one replicate of 5 fish per dose level. Fish were exposed to nominal test concentrations of 50, 30.0, 18.0, 10.8, 6.48, 3.89 mg/L, and a water control. Fish mortality was observed in 20% of the fish exposed to 3.89 mg/L, 60% of the fish at 6.48 mg/L, and 100% of the fish at 10.8 mg/L and higher. There was no mortality or other effects observed in the water controls. Based on this information, the target or nominal concentrations selected for the definitive test were 0.653, 1.33, 2.19, 3.50, 5.91, and 10.0 mg butyl propionate/L, and a water control.

Ten fish (5 fish per replicate; two replicates per dose level) were exposed to nominal test concentrations of n-butyl propionate at nominal target concentrations of 0.653, 1.33, 2.19, 3.50, 5.91, and 10.0 mg butyl propionate/L, plus a water control. Fish were added to each test vessel within 30 minutes of solution preparation and initial test solution sampling. The concentration butyl propionate was confirmed by collecting test solution samples on days 0 and 4 from each test vessel. Test concentrations for day 0 replicate test solutions ranged from 95.6 to 105% of target concentrations. Day 4 measured concentrations ranged between 76.6 and 93.1% of target . The overall average percent of nominal for the entire study was 86.1 to 94.8%. The resulting mean measured n-butyl propionate concentrations were 0.562, 1.30, 1.92, 3.22, 5.60, and 9.45 mg/L.

Samples of the initial test solutions were analyzed by gas chromatography analysis using an Agilent 6890N gas chromatograph equipped with a flame ionization detector (FID) (standard preparation, detector calibration, instrument conditions for analysis described in detail in report). Replicates were

analyzed at the start of the study and at 96 hours at test termination.

Statistical analysis: The U.S. EPA Trimmed Spearman-Karber Program, Version 1.5 was used to calculate the LC_{50} values, confidence limits, and corresponding trim values. Values were determined using mean measured concentrations. The NOEC was determined based on biological interpretation of the data and the highest exposure level exhibiting no fish mortality or sub lethal effects.

Results: Day 0 analysis of test solutions for butyl propionate demonstrated that dose solutions ranged from 95.6 to 105% of target nominal values; Day 4 (96 hr) analysis of replicate test solutions yielded percent of nominal values ranging from 76.6 to 93.1% The overall average percent of nominal was 86.1 to 94.8%. Mean measured concentrations were calculated for all dose levels by averaging the day 0 concentrations and day 4 exposure solution concentrations (see table below).

Results of Analysis of Test Solutions for n-Butyl Propionate

Target Concentration (mg/L)	Day 0 Mean Solution Concentrations (mg/L)	Day 4 Mean Solution Concentrations (mg/L)	Mean Measured Concentations[1] (mg/L)
Control	<LLQ[2]	<LLQ	NA[3]
0.653	0.624	0.500	0.562
1.33	1.40	1.19	1.30
2.19	2.07	1.77	1.92
3.50	3.38	3.06	3.22
5.91	5.70	5.50	5.60
10.0	9.75	9.15	9.45

1: Mean measured concentration = mean of day 0 and day 4 concentration values
2: less than Lowest Level Quantified: 0.452 mg n-butyl propionate/L
3: Not Applicable

Observations were made for mortality (no response to contact with the caudal peduncle and no opercula movement), behavioral effects (lethargy, hyperactivity, swimming at surface, complete or partial loss of body equilibrium, erratic movement) and gross pathological effects (exophthalmia, ascites, hemorrhage, excess mucus, sloughing of epidermis, melanosis) in response to exposure to n-butyl propionate. There was a dose-response effect observed in fish in response to n-butyl propionate (see table below).

Biological Response to n-Butyl Propionate Exposure in Fish

Target	Mean Measured	Biological Resonse Observed

Concentration (mg/L)	Concentation (mg/L)	24 hours	48 hours	72 hours	96 hours
Control	NA[3]	10N	10N	10N	10N
0.653	0.562	10N	10N	10N	10N
1.33	1.30	10N	10N	10N	10N
2.19	1.92	10N	9N, 1PE	9N, 1PE	9N, 1CE
3.50	3.22	10N	9N, 1L	10N	10N
5.91	5.60	10N	10N	7N, 3L	5L, 4PE, 1D
10.0	9.45	4N, 1L, 4PE, 1CE	2PE+L, 1CE, 7D	1PE, 9D	10D

N = normal; L = lethargic; D = dead; PE = partial loss of equilibrium; CE = complete loss of equilibrium; I = immobility
2: Less than Lowest Level Quantified: 0.80 mg/L

No mortality was observed at concentrations of 3.22 mg/L and below or in the water control. Sublethal effects were observed at concentrations as low as 1.92 mg/L during the conduct of the test. Sublethal effects observed included partial or complete loss of equilibrium and lethargy. No sublethal effects were observed at 1.30 mg.L or lower concentrations. There is some uncertainty whether the effects observed at the 1.92 and 3.22 mg/L test concentrations were actual toxic effects from exposure to the test material or if they were only incidental effects. One fish (10%) at each of these test concentrations was affected. Based on these results, the NOEC for this study was empirically determined as the concentration immediately below the region of uncertainty (1.92 and 3.22 mg/L), which results in a conservative (lowest value) estimation of the NOEC.

The 24-hour LC_{50} value was greater than the highest exposure concentration tested of 9.45 mg/L.

The 48-hour LC_{50} value, calculated by the U.S. EPA Trimmed Spearman-Karber Program, was each 8.14 mg/L; no reliable 95% confidence interval could be determined. The Spearman-Karber trim was 30%.

The 72-hour LC_{50} value,calculated by the U.S. EPA Trimmed Spearman-Karber Program, was 7.49 mg/L; no reliable 95% confidence interval could be determined. The Spearman-Karber trim was 10%.

The 96-hour LC_{50} value, calculated by the U.S. EPA Trimmed Spearman-Karber Program, was 6.89 mg/L with a 95% confidence interval of 6.22-7.63 mg/L. The Spearman-Karber trim was 0%.

		The 96-hour NOEC was 1.30 mg/L and was determined based on biological interpretation of the data and the highest exposure level exhibiting no mortality or sub-lethal effects.
	Reliability:	score = 1; valid without restriction. GLP guideline study
	Reference:	Marino, T.A, McClymont, E.L., and Yaroch, A.M. 2005. n-n-Butyl Propionate: An Acute Toxicity Study with the Rainbow Trout, *Oncorhynchus mykiss* (unpublished study). Toxicology & Environmental Research and Consulting, Study ID 051124. The Dow Chemical Company, Midland, MI.

(b)	Type:	static
	Species:	*Pimephales promelas* (fathead minnow)
	Unit:	mg/l
	Exposure Period:	96 hour
	NOEC:	
	LC0:	
	LC50:	43
	LC100:	
	Analyt. Monitoring:	no data
	Method other:	USEPA. 1985. Methods for Measuring the Acute Toxicity of Effluents to Freshwater and Marine Organisms. EPA/600/4-85/013, dated March, 1985.
	GLP:	no
	Test substance:	n-butyl propionate, purity not specified
	Remark:	Ten fish (1.5-3.0 cm in length) were exposed per test concentration in a total volume of 750 ml. Replicates were prepared for each concentration. Five concentrations of n-butyl propionate were tested (nominal concentrations between 25 and 150 mg/l) and an untreated control. Test concentrations selected were based on initial 24-hour range-finding studies which utilized 2 to 3 fish per concentration. Dechlorinated muncipal wastewater treated with activated charcoal was utilized to maintain fish and as dilution water. Water analysis indicated total hardness was 40-60 mg/l as $CaCO_3$; pH was approximately 7.0 SU. Temperature, fish survival, pH, and dissolved oxygen were monitored during the 96-hour test interval. Dissolved oxygen was maintained above 4 mg/l by the use of control by minimal aeration which was initiated after the first 4 hours of testing. LC50 and confidence limit values were obtained using the Trimmed Spearman-Karber method.
	Results:	The 96-hour LC50 in fathead minnows was determined to be 43.0 mg/l.
	Confidence limits:	95% confidence limits: 40.9 – 45.2 mg/l
	Reference:	Waggy, G.T. 1989. Ecological Fate and Effects Testing of UCC Products and Wastewaters During 1988 (unpublished report). File No. 37073. Project report dated June 27, 1989. Union Carbide Corporation, South Charleston, WV.

(b)	Type:	static
	Species:	Sheepshead minnow
	Unit:	mg/l
	Exposure Period:	96 hour
	NOEC	
	LC0:	
	LC50:	61
	LC100:	
	Analyt. Monitoring:	no data
	Method:	
	Year:	
	GLP:	no data
	Test substance:	n-butyl propionate
	Reliability	score = 4; insufficient documentation for assessment
	Reference:	Union Carbide Corporation. Material Safety Data Sheet # 837: UCAR™ n-Butyl Propionate. Effective date 06/07/2001. Union Carbide Chemicals and Plastics Technology Corporation, The Dow Chemical Company, Danbury, CT.

(c)	Value:	12.962 mg/L
	Remark:	An acute fish 96-hr LC50 was calculated using ECOSAR from the USEPA. The SAR for esters was used. The structure was determined from the CAS RN as stpred om the accp,[amuomg database pf SMILES notations within ECOSAR. Parameter values used for modelling were: molecular weight: 130.19 g/mol; log Kow: 2.34 (calculated); melting point: -89 °C; water solubility: 1428 mg/L; calculated by EPIWIN)
	Reliability:	score = 2, valid with restriction; accepted calculation method
	Reference:	USEPA ECOSAR Version 0.99f). 2000. EPISUITE v. 3.10. U.S. Environmental Protection Agency.

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

A. Daphnia

(a)	preferred result	reliability = 1, valid without restrictions. GLP guideline study
	Type:	flow-through
	Test:	EC50 (immobilization)
	Species:	*Daphnia magna* Straus, freshwater invertebrate
	Unit:	mg/L
	Exposure Period:	48 hours
	LC50:	18.5
	NOEC:	5.56
	Test substance:	n-butyl propionate, purity 99.7%
	Analyt Monitoring.:	yes

Year:	1992
GLP:	yes
Methods:	OECD Guideline for Testing of Chemicals No. 202, *Daphnia sp.*, Acute Immobilization Test, Part 1. Adopted 13 April 2004. Annex to Commission Directive 92/69/EEC, C.2 Acute Toxicity for *Daphnia*, Vol. 35. 29 December 1992 U.S. Environmental Protection Agency. Daphnid Acute Toxicity Test 40CFR797.1300. July 1, 1992. The test organism, *Daphnia magna* Straus, was originally obtained from New England Bioassay, Inc., Manchester, CT. Daphnid instars less than 24 hours old from laboratory-reared cultures were used as the test organism. Dapnid cultures were maintained under illumination (cool-white fluorescent, 2050 + 350 lux) on a 16-hour light/8-hour dark photoperiod at a temperature of 20 + 2 °C. Daphnids were fed a mixed diet of freshwater green algae (*Pseudokirchneriella subcapitata*, formerly known as *Selenastrum capricornutum*) and YCT (yeast, Ceraphyll, and trout chow suspension) five times per week. First instar daphnids (< 24-hr old) were separated from adults and older instars on the day of testing by gentle screening through a nylon mesh and metal sieve. Laboratory water was obtained from the upper Saginaw Bay of Lake Huron; before use, water was sand-filtered, pH-adjusted with carbon dioxide, carbon-filtered, and UV-irradiated. Water quality parameters of laboratory water were as follows: Hardness (mg $CaCO_3$/L): 71 Alkalinity (mg $CaCO_3$/L): 42 Conductivity (umhos/cm): 169 Residual chlorine: <10 ppb Definitive testing was conducted in 600 ml glass beakers with a test solution volume of 500 ml. Each beaker contained a screen-covered glass protrusion exit port at approximately 500 ml graduation mark to allow for the overflow of test solution during each cycle of the dilution system. An intermittent-flow proportional diluter system weas used to maintain constant exposure concentrations during the 48-hour study interval. The system is designed to deliver up to six (6) test concentrations as well as a vehicle and water control. The dosing system (Microlab® 500 Dosing System, Hamilton Company, Reno, NV) delivered a designated amount of undiluted test material from a glass vessel to the mixing chamber where it was mixed with laboratory dilution water. When the system cycled, the test solution was delivered to its respective test vessel. Two replicate test vessels were prepared for each exposure concentration. Two additional vessels with no test material added were used as water controls. Vessels were replenished with test solutions on a regular intermittent cycle of approximately every 45 minutes.

The dilution system was calibrated prior to initiation of the test. Test vessels were placed in a water trough equipped with a thermostatic temperature controller which maintained a water temperature of 20 + 1 °C. Daphnids were not fed during the test. Daphnids were observed for immobility (inability to swim within 15 seconds after gentle agitation of the test container) after 24 and 48 hours of exposure.

n-Butyl propionate nominal test concentrations for the definitive test were selected based on a 48-hour static probe study. The study was conducted with one replicate of 10 *Daphnia* per dose level exposed to butyl propionate concentrations of 0, 15.6, 25.9, 43.2, 72.0, 120, and 200 mg/L. After 48 hours exposure, there was 100% daphnid immobility at and above 72 mg/L; there was 4%, 30%, and 70% immobility at 15.6, 25.9, and 43.2 mg/L, respectively. There were no changes in behavior, and no immobility observed in water controls.

In the definitive test, twenty *Daphnia* (10 per replicate; two replicates per dose level) were exposed to nominal test concentrations of butyl propionate of 5.44, 9.07,, 15.1, 25.2, 42.0, and 70.0 mg/L plus a water control. These nominal target concentrations were equivalent to mean measured concentrations of 3.09, 5.56, 10.4, 17.2, 33.5, and 49.1 mg butyl propionate/L, respectively. Replicate test solutions were sampled for analytical confirmation on day 0 and day 2 of the study using an Agilent 6890 N gas chromatograph equipped with a flame ionization detector (FID). To assess analytical method precision and solution homogeneity, three additional samples were taken on day 0 from representative 5.44 and 70.0 mg/L test solutions. Calibration with analytical standards was performed prior to analysis of each respective set of test solution samples. The standard deviation for daily calibrations did not exceed 10%; the GC/FID instrumentation exhibited a linear response over the calibration range of 0.23 to 43 mg butyl propionate/L (standard preparation, detector calibration, instrument conditions for analysis described in detail in report).

Statistical analysis: Because there was an insufficient number of test concentrations that resulted in immobilization, the USEPA Probit Program Version 1.5 could not be used for the statistical evaluation of the biological data for the 24-hour time point of this study. Therefore, using mean measured n-butyl propionate concentrations, the USEPA Trimmed Spearman-Karber Program TSK), Version 1.5 was used to calculate the 24-hr EC50 value and corresponding percent trim values. The USEPA Probit Program, Version 1.5 was used to calculate the 48-hr EC50value. The NOEC was determined based on biological

interpretation of the data and the highest exposure level exhibiting no *Daphnia* immobility.

Results: Day 0 analysis of test solutions for n-butyl propionate demonstrated that dose solutions ranged from 59.2% to 87.6% of target nominal values. Day 2 (48 hr) analysis of test solutions yielded percent of nominal values ranging from 54.2 to 71.1%. Mean measured concentrations were calculated for all dose levels by averaging the day 0 concentrations and day 2 exposure solution concentrations (see table below).

Results of Analysis of Test Solutions for n-Butyl Propionate

Target Concentration (mg/L)	Day 0 Solution Concentrations* (mg/L)	Day 2 Solution Concentrations* (mg/L)	Mean Measured Concentations[1] (mg/L)
Control	<LLQ[2]	<LLQ	NA[3]
5.44	3.22	2.95	3.09
9.07	5.46	5.66	5.56
15.1	10.9	9.81	10.4
25.2	17.9	16.4	17.2
42.0	36.8	30.1	33.5
70.0	49.0	49.1	49.1

*Average of two replicate test solutions
1: Mean measured concentration = mean of day 0 and day 2 concentration values
2: less than Lowest Level Quantified: 0.906 mg/L
3: Not Applicable

pH values ranged from 7.6 to 7.9. Temperature during the test remained constant at .20 °C; light intensity 739-950 lux. Dissolved oxygen was between 7.9-8.9 mg/L (89-100% oxygen saturation).

Observations were made for immobility in response to exposure to n-butyl propionate. At 24 and 48 hours, no immobility was observed the two lowest test concentrations or in the water control. There was a dose-dependent increase in immobility at higher concentrations (see table below); at 48 hours, there was 100% immobility at the highest test concentration.

Biological Response to Butyl Propionate Exposure

Target Concentration (mg/L)	Mean Measured Concentation[1] (mg/L)	Biological Response Observed	
		24 hours	48 hours
Control	<LLQ[2]	20N	20N
5.44	3.09	20N	20N
9.07	5.56	20N	20N
15.1	10.4	17N, 3I	16N, 4I

25.2	17.2	8N, 12I	8N, 12I
42.0	33.5	12N, 8I	7N, 13I
70.0	49.1	9N, 11I	20I

N = normal; I = immobile.
1: Mean measured concentration = mean of day 0 and day 2 concentration values
2: less than Lowest Level Quantified: 0.906 mg/L

Based mean measured n-butyl propionate concentrations:
The 24-hour EC50 value, calculated by the U.S. EPA trimmed Spearman-Karber Program, was 25.9 mg/L, with a 95% confidence interval of 5.59 to >49.1 mg/L. The Spearman-Karber trim was 45%.
The 48-hour EC50 value, calculated by the U.S. EPA Probit Program, was 18.5 mg/L, with a 95% confidence interval of 15.0 to 22.7 mg/L. The Probit slope was 3.6 (95% confidence interval 2.5-4.7).

The 48-hour NOEC was 5.56 mg/L and was determined based on the highest exposure level exhibiting no dapnid immobility or change in behavior or appearance.

Reference: Marino, T.A, Najar, J.R., and Sushynski, B.S 2005. n-Butyl Propionate: An Acute Toxicity Study with the Daphnid, *Daphnia magna* (unpublished study). Toxicology & Environmental Research and Consulting, Study ID 051067. The Dow Chemical Company, Midland, MI.

(b)

Type:	static
Species:	*Daphnia magna*.(water flea)
Unit:	mg/l
Exposure Period:	48 hours
NOEC:	
LC0:	
LC50:	86
LC100:	
Analyt. Monitoring:	no data
Method other:	USEPA. 1985. Methods for Measuring the Acute Toxicity of Effluents to Freshwater and Marine Organisms. EPA/600/4-85/013, dated March, 1985.
GLP:	no
Test substance:	n-butyl propionate, purity not specified
Remark:	*Daphnia* neonates less than 24-hr old (first instar) were used exposed to a series of 5 to 10 geometrically equidistant concentrations of n-butyl propionate plus an untreated control. *Daphnia* neonates were obtained from gravid females which were kept isolated for approximately 20 hours. *Daphnia* were from a culture that originated from a USEPA laboratory in Duluth, MN. Cultures were maintained at 19-23 degree C and

		fed laboratory-prepared food consisting of pulverized trout food, yeast and alfalfa powder. Analysis of water used to maintain cultures and as dilution water indicated total hardness as 40 – 60 mg/l as $CaCO_3$, total alkalinity as 25 – 38 mg/l as $CaCO_3$, pH 7.0 – 7.2 SU, and conductivity 250 umhos/cm. Dissolved oxygen and pH were determined at test initiation and at 48 for all test concentrations and controls. Mortality was recorded at 24 and 48 hours. LC50 and confidence limit values were obtained using the Trimmed Spearman-Karber method.
	Results:	The 48-hr LC50 in Daphnia magna is 86.2 mg/l
	Confidence limits:	95% confidence limits: 73.8 – 100.7 mg/l
	Reference:	Waggy, G.T. 1989. Ecological Fate and Effects Testing of UCC Products and Wastewaters During 1988 (unpublished report). File No. 37073. Project report dated June 27, 1989. Union Carbide Corporation, South Charleston, WV.
(c)	Value:	50.179 mg/L
	Remark:	An acute Daphnia 48-hr LC50 was calculated using ECOSAR from the USEPA. The SAR for esters was used. The structure was determined from the CAS RN as stpred om the accp,[amuomg database pf SMILES notations within ECOSAR. Parameter values used for modelling were: molecular weight: 130.19 g/mol; log Kow: 2.34 (calculated); melting point: -89 °C; water solubility: 1428 mg/L; calculated by EPIWIN)
	Reliability:	score = 2, valid with restriction; accepted calculation method
	Reference:	USEPA ECOSAR Version 0.99f). 2000. EPISUITE v. 3.10. U.S. Environmental Protection Agency.

B. Other

(a)	Type:	static
	Species:	Mysid shrimp
	Unit:	mg/l
	Exposure Period:	96 hours
	TLm	
	LC0:	
	LC50:	100 mg/l
	LC100:	
	Analyt. Monitoring:	no data
	Method:	
	Year:	
	GLP:	no data
	Test substance:	n-butyl propionate
	Remark:	reliability score = 4, documentation insufficient for assessment
	Reference:	Union Carbide Corporation. Material Safety Data Sheet # 837:

UCAR™ n-Butyl Propionate. Effective date 06/07/2001. Union Carbide Chemicals and Plastics Technology Corporation, The Dow Chemical Company, Danbury, CT.

4.3 TOXICITY TO AQUATIC PLANTS e.g. Algae

(a)	preferred result	reliability = 1, valid without restrictions
	Type:	static
	Test:	EC50, based growth inhibition (cell density)
	Species:	Pseudokirchneriella subcapitata (formerly know as Selenastrum capricornutum), freshwater green algae
	Unit:	mg/L
	Exposure Period:	96 hours
	EC25:	134
	EC50:	261
	NOEC:	82.2
	Test substance:	n-butyl propionate (CAS No. 590-01-2), purity 99.92%
	Analyt Monitoring.:	yes
	Year:	2003
	GLP:	yes
	Method:	OECD Guideline 201, Algal Growth Inhibition Test EEC Directive 92/69/EEC, C.3 Algal Inhibition Test USEPA Algal Acute Toxicity Test 40CFR797.150/revision of TSCA guidelines Federal Register Vol 50 No.188. The green alga Pseudokirchneriella subcapitata (formerly know as Selenastrum capricornutum) was maintained in the laboratory and originated from the University of Toronto Algal Collection, Toronto, Ontario,Canada. Algal cultures were maintained in algal assay medium (AAM) designed by Miller et al. for the EPA Algal Assay Bottle Test (EPA-600/9-78-018.5) in flasks under continuous cool-white fluorescent illumination of 7509 ± 435 lux at 24.8 ± 01°C and continuously shaken at 100 oscillations per minute. Algal assay medium (AAM) was prepared by adding requisite amounts of each of the macro- and micro-nutrients into de-ionized water (compete description provided in report) . After pH adjustment to 7.5±0.1 S.U., the media was filtered using a 0.45 micrometer porosity filter and stored in the dark at approximately 4°C. AAM was used for toxicity tests and maintenance of algal stock cultures. Test solutions were prepared by direct addition of the test substance to the test medium without pH adjustment. Nominal concentrations of 4.10, 10.2, 25.6, 60.1, 164, 400, and 1000 mg n-butyl propionate plus a medium control. These nominal concentrations were equivalent to mean measured concentrations of 1.97, 4.51, 12.4, 30.2, 82.2, 152, and 434 mg butyl propionate, respectively. Butyl propionate test concentrations were selected based on a range-finding test. In

the range-finding assay, the percent decrease in cell density across test concentrations (0.10 to 100 mg/L) was -4 to 60% (negative percent indicates stimulation of growth).

Test vessels were sterilized 250-mL Erlenmeyer flasks fitted with Shimadzu closures, each containing 100 ml assay medium. Three replicates flasks were prepared for each concentration; an additional flask was not inoculated with algae and served as a control blank. At test initiation and termination, the pH was measured for each test concentration and control blank replicates. Each flask (except the fourth control blank flask) was inoculated with 0.71 mL of the algae containing approximately 1.0 E+6 cells/mL, resulting in an initial cell density of approximately 1.0 E+4 cells/mL. The agal inoculum was prepared from a 3-day old stock culture. Flasks were placed in an environmental chamber and maintained at 24.1 $\pm$ 1 °C under continuous illumination at 7766 $\pm$ 435 lux and continuously shaken at 100 oscillations/ minute. Light intensity was measured daily at positions corresponding to the test flasks in the incubator chamber; temperature was monitored continuously during the test interval.

Algal cell counts were determined by electron particle counting using a Coulter Multisizer 3. Total cell counts were determined at approximately 24, 48, 72, and 96 hours. Three separate cell count reading were made per replicate. At test termination, algal cell morphology was microscopically evaluated at 20x or 40x magnification in a hemacytometer counter chamber.

Samples of the initial test solutions were analyzed for butyl propionate concentration using Agrilent 6890N GC equipped with a flame ionization detector. Replicates were also analyzed at 96 hours at test termination.

Statistical analysis: study endpoints were evaluated based on the mean measured butyl propionate concentrations and are expressed in terms of algal growth (cells per ml). Endpoints analyzed were cell density, growth rate per day, and biomass (area under the growth curve). EC50 values for cell density were determined by a least squares linear regression of cell density against the log of the concentration at 72 and 96 hours. The $EC_{gr}50$ value for growth inhibition was calculated by regressing the percent reduction in mean specific growth rate for each dose group compared to the control group against the natural logarithm of the concentrations for the 0-72 hr and 0-96 hr exposure intervals. The $EC_{bm}50$ value for biomass inhibition was calculated by regression of the differences in area under the growth curves for each dose compared to the control against the log of the concentrations for 72 and 96 hours. Prior to evaluation of NOEC concentrations, data were tested for normality using the Shapiro-Wilk's Test and for homogeneity of variance using the Bartlett's Test. To meet assumptions of

normality and/or homogeneity, the 96-hr cell density and 96-hr biomass data were log transformed. The 72- and 96-hour NOEC values for cell density, growth rate, and biomass (area under growth curve) were calculated using the analysis of variance and Dunnett's test ($\alpha = 0.05$).

Results:

Day 0 analysis of test solutions for n-butyl propionate demonstrated dose solutions ranged from 76% to 103% of target values. Day 4 (96 hr) test solutions yielded no quantifiable concentrations of butyl propionate in test solutions with or without algae. Mean measured concentrations were calculated for all dose levels by averaging the day 0 concentrations and day 4 exposure solution concentrations. Since day 4 measured concentrations were all less than the lowest level quantified (LLQ = 0.656 mg/L), a value of 0.328 mg/L (one-half the LLQ) was used in calculations as a conservative estimate of day 4 concentrations (see table below).

Results of Analysis of Test Solutions for Butyl Propionate

Target Concentration (mg/L)	Day 0 Solution Concentrations* (mg/L)	Day 4 Solution Concentrations (mg/L)	Mean Measured Concentations[1] (mg/L)
Control	<LLQ[2]	<LLQ	NA[3]
4.10	3.61	<LLQ	1.97
10.2	8.70	<LLQ	4.51
25.6	24.5	<LLQ	12.4
64.0	60.1	<LLQ	30.2
160	164	<LLQ	82.2
400	304	<LLQ	152
1000	867	<LLQ	434

*Average % of target dose on Day 0: 89.8 ± 8.65

1: Mean measured concentration = mean of day 0 and day 4 concentration values

2: less than Lowest Level Quantified: 0.656 mg/L

3: Not Applicable

With the exception of the highest dose, pH values ranged from 7.6 to 7.3 at test initiation, and from 9.1 to 9.7 in replicates with algae at test termination, and from 7.2 to 7.4 in blank control replicates without algae at test termination. Despite the increase pH in agal cultures, the integrity of the test was deemed unaffected, since the control performance was unaffected (see table below).

Mean Cell Density after 72 and 96 Hours

Butyl Propionate (mg/L)[1]	Mean Cell Density (x104 cells/ml)			
	72 hr	% Inhibit[3]	96 hr	% Inhibit
<LLQ[2]	214.7	NA[4]	492.7	NA
1.97	228.5	-6[5]	505.6	-3
4.51	250.2	-17	515.1	-5
12.4	187.0	13	303.2	38
30.2	214.5	0	480.7	2

82.2	187.4	13	442.1	10
152	132.6	38	383,7	22
434	0.634	100	3.06	99

1: Mean measured concentration = mean of day 0 and day 4 concentration values
2: less than Lowest Level Quantified: 0.656 mg/L
3: % inhibition relative to control value at 72 or 96 hours
4: Not Applicable
5: negative value indicates growth stimulation

Based mean measured n-butyl propionate concentrations, the 72 hour results were as follows:
72-hr EC25 = 109 mg/L based on cell density
72-hr EC50 = 175 mg/L based on cell density
72-hr $EC_{bm}50$ = 166 mg/L based on biomass (area under the growth curve)
72-hr $EC_{gr}50$ = 204 mg/L based on growth rate per day
72-hr NOEC = 82.2 mg/L for all three criteria

Based mean measured n-butyl propionate concentrations, the 96 hour results were as follows:
96-hr EC25 = 134 mg/L based on cell density
96-hr EC50 = 239 mg/L based on cell density
96-hr $EC_{bm}50$ = 182 mg/L based on biomass (area under the growth curve)
96-hr NOEC = 82.2 based on cell density and biomass
96-hr $EC_{gr}50$ = 261 mg/L based on growth rate per day
96-hr NOEC = 152 mg/L based on growth rate per day

Reference: Hancock, G.A., McClymont, E.L., Hales, C.A., and Staley, J.L. 2003. UCAR™ n-Butyl Propionate: Growth Inhibition Test with the Freshwater Green Algaa, *Pseudokirchneriella subcapitata* (unpublished study). Toxicology & Environmental Research and Consulting, Study ID 021136. The Dow Chemical Company, Midland, MI.

(b) Value: 1.045 mg/L
Remark: An acute green algae 96-hr LC50 was calculated using ECOSAR from the USEPA. The SAR for esters was used. The structure was determined from the CAS RN as stpred om the accp,[amuomg database pf SMILES notations within ECOSAR. Parameter values used for modelling were:
molecular weight: 130.19 g/mol;
log Kow: 2.34 (calculated);
melting point: -89 °C;
water solubility: 1428 mg/L; calculated by EPIWIN)
Reliability: score = 2, valid with restriction; accepted calculation method
Reference: USEPA ECOSAR Version 0.99f). 2000. EPISUITE v. 3.10. U.S. Environmental Protection Agency.

4.4 TOXICITY TO BACTERIA

(a)	Preferred value	(reliability score = 2, valid with restrictions)
	Type:	aerobic
	Species:	bacteria, non-acclimated derived from domestic wastewater
	Unit:	mg/l
	Exposure Period:	16 hour
	EC0:	
	EC10:	
	EC50:	508
	Analyt. Monitoring:	no data
	Method other:	Alsop, G.M., Waggy, G.T., and Conway, R.A. 1980. Bacterial growth inhibition test. Journal Water Pollution Control Federation, Volume 52, October 1980.
	GLP:	no
	Test substance:	n-butyl propionate, purity not specified
	Remark:	n-Butyl propionate was evaluated at selected concentrations with microorganisms derived from settled domestic wastewater. The test material, seed microorganisms, buffered dilution water, and a nutrient solution of yeast extract and sodium acetate were added to round bottomed bottles. Control bottles were run concurrently to measure growth and turbidity in the absence of the test material. Bottles were stoppered with cotton plugs and then placed on a platform shaker at ambient temperature of 22 $\pm$ 2 degree C for 16 hours. At the end of the 16-hour interval, the degree of inhibition induced by the test material was assessed by measuring the turbidity level of each bottle (optical density at 530 nm). Measured optical density was calculated as a percentage of the seeded growth in control bottles. The percent of control values for each test concentration was plotted against the log of the test sample concentration; the test concentration which corresponded to 50% of the control value was the 50% Inhibition Concentration (IC50).
	Result:	The median inhibition concentration (IC50) for n-butyl propionate in bacteria was determined to be 508 mg/l.
	Reference:	Waggy, G.T. 1989. Ecological Fate and Effects Testing of UCC Products and Wastewaters During 1988 (unpublished report). File No. 37073. Project report dated June 27, 1989. Union Carbide Corporation, South Charleston, WV.

4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS

4.5.1 CHRONIC TOXICITY TO FISH

No data available

4.5.2. CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

No data available

4.6 TOXICITY TO TERRESTRIAL ORGANISMS

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

No data available

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

No data available

4.6.3 TOXICITY TO OTHER NON MAMMALIAN TERRESTRIAL SPECIES (INCLUDING AVIAN)

No data available

4.7 BIOLOGICAL EFFECTS MONITORING (INCLUDING BIOMAGNIFICATION)

No data available

4.8 BIOTRANSFORMATION AND KINETICS

No data available

4.9 ADDITIONAL REMARKS

5.0 TOXICITY

5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

(a)	Preferred (male) value:	reliability score = 1, valid without restriction; comparable to guideline study
	Type:	LD50
	Species/strain:	rat/Sprague-Dawley/male
	Value:	14.1 ml/kg (12,344 mg/kg)
	Method:	Male Sprague-Dawley rats (200-300 grams) received 4.0, 8.0, 11.2, or 16 ml/kg (3502, 7004, 9806, or 14,008 mg/kg) of n-butyl proprionate in a single dose by stomach intubation. The rats were fasted overnight prior to dosing. Animal weights were recorded at 0, 7 and 14 days. The group size at each dose level was 5 animals/group. Animals were observed for evidence of toxicity immediately after dosing and throughout the 14-day observation interval. The LD50 value was calculated by the moving average method (Thompson, 1947; Weil, 1983) after the animals had been observed for 14 days for clinical signs and survival. A gross pathology exam was conducted on animals found dead or at sacrifice.
	Year:	1988
	GLP:	no
	Test substance:	n-butyl propionate, >99% purity

Remark:	Four of the 5 male rats receiving n-butyl propionate at the maximum peroral dose of 16 ml/kg (14,008 mg/kg) died after one day. The survivor recovered at four days. Signs of toxicity included sluggishness at 15 minutes after dosing, unsteady gait at 30 minutes, lacrimation, and prostration and 1.0, and 1.5 hr, respectively. A slight red crust on perinasal and periocular fur was noted at 1 day. No mortality occurred in animals receiving lower doses. Animals dosed at 11.2 ml/kg demonstrated slight sluggishness at 2.0 hr, but recovered at 1 day. There were no signs of toxicity observed at the lower dosages. Weight gain in surviving animals from all groups was normal. At necropsy, mottled lungs, discolored stomachs filled with clear fluid, and mottled kidneys were observed in rats dying on study. Survivors at all dosages had no remarkable gross lesions.
Result:	The LC50 for n-butyl propionate in male Sprague Dawley rats (with 95% confidence limits) = 12,344 (10593 – 14,383) mg/kg body weight
Reference:	Myers, R.C. 1988. Union Carbide Corporation (unpublished report), UCAR® n-Butyl Propionate, Acute Toxicity and Primary Irritancy Studies. Bushy Run Research Center, Project Report 51-68, July 27, 1988.

(b) Preferred (female) value: reliability score = 1, valid without restrictions, comparable to guideline study.

Type:	LD50
Species/strain:	rat/Sprague-Dawley/female
Value:	12.6 ml/kg (11,031 mg/kg)
Method:	Female Sprague-Dawley rats (200-300 grams) received 8.0, 11.2, or 16 ml/kg (7004, 9806, or 14008 mg/kg) of n-butyl proprionate in a single dose by stomach intubation. The rats were fasted overnight prior to dosing. Animal weights were recorded at 0, 7 and 14 days. The group size at each dose level was 5 animals/group. Animals were observed for evidence of toxicity immediately after dosing and throughout the 14-day observation interval. The LD50 value was calculated by the moving average method (Thompson, 1947; Weil, 1983) after the animals had been observed for 14 days for clinical signs and survival. A gross pathology exam was conducted on animals found dead or at sacrifice.
Year:	1988
GLP:	no
Test substance:	n-butyl propionate, >99% purity
Remark:	All five female rats receiving butyl propionate at the maximum peroral dose of 16 ml/kg (14,008 mg/kg) died after one day. Signs of toxicity included sluggishness, unsteady gait and lacrimation at 30 minutes after dosing, and prostration at 3 hours. One of 5 rats dosed at 11.2 ml/kg (9893 mg/kg) died on day 1; all rats demonstrated slight unsteady gait and sluggishness at 2.0 hr,

survivors recovered at 1 day. Slight sluggishness was observed at 2 hours among rats receiving the lowest dose, 8 ml/kg (7004 mg/kg); all animals recovered after 1 day. Weight gain in surviving animals from all groups was normal. At necropsy, mottled lungs, discolored stomachs filled with clear fluid, intestines filled with clear fluid, and mottled kidneys were observed in rats dying on study. Survivors at all dosages had no remarkable gross lesions.

Result: The LC50 for n-butyl propionate in female Sprague Dawley rats (with 95% confidence limits) = 11,031 (9369 – 12,957) mg/kg body weight

Reference: Myers, R.C. 1988. Union Carbide Corporation (unpublished report), UCAR® n-Butyl Propionate, Acute Toxicity and Primary Irritancy Studies. Bushy Run Research Center, Project Report 51-68, July 27, 1988.

(c)

Type: LD50
Species: rat/Fischer 344
Value: >5000 mg/kg
Method: OECD Test Guideline 401
One group of five male and five female Fischer 344 rats (8-9 weeks old) was fasted overnight, weighed, and given a single dose of n-butyl propionate by gavage, using a ball pointed cannula and syringe. The test material was administered undiluted at a dose volume of 5.71 ml/kg (5000 mg/kg based on density 0.8755 g/ml). Approximately three hours after dosing on Day 1 animals were allowed food ad libitum. Clinical examinations were made three times daily for the first three days and once daily thereafter for the remainder of the 14-day observation interval. The initial (Day 1), Day 7, and Day 14 bodyweights were recorded and changes in body weights calculated.
Year: 1988
GLP: no
Test substance: n-butyl propionate, 99.825%
Remark: There was no mortality or clinical signs observed in any of the rats receiving a one-time dose of 5000 mg/kg n-butyl propionate. All rats gained weight during the 14-day observation interval.
Result: The LD50 for male and female Fischer 344 rats is greater than 5000 mg/kg body weight.
Reliability: score = 1, valid without restrictions; OECD guideline study
Reference: Gardner, J.R. 1989. Shell Chemical Company, London, (unpublished report), N-Butyl Propionate: Acute Oral and Dermal Toxicology, Skin and Eye Irritancy and Skin Sensitising Potential. Sittingbourne Research Center Laboratory Number SBGR 88.195, March 13, 1989.

(d)

Type: LD50

Species:	rat/Wistar
Value:	>16 ml/kg (14008 mg/kg)
Method other:	Groups of five non-fasted male Wistar rats (90-120 g, 3-4 weeks old) received n-butyl propionate by gavage at dosages of 64, 32, 16, and 4 ml/kg (56,032, 28016, 14,008, and 3502 mg/kg). Animals were weighed prior to dosing and at Day 14 and changes in body weights recorded. Clinical observations were performed immediately after dosing and throughout Day 0 (day of dosing), and throughout the 14 day observation interval. Animals were sacrificed on Day 14. A gross pathology exam was conducted on animals found dead or at sacrifice.
Year:	1976
GLP:	no
Test substance:	n-butyl propionate
Remark:	All animals in the 64 and 32 ml/kg dosage groups died within two days of dosing. Signs of toxicity included sluggishness, deep breathing, unsteady gate, and prostration. There were no deaths in the lower dose groups; the only sign of toxicity was transient sluggishness. Surviving animals gained weight during the 2-week observation interval. At necropsy, animals dying on study had mottled and slightly congested kidneys, and distended and liquid-filled stomachs and intestines. No gross lesions were observed in animals from the lower dose groups.
Result:	The LD50 for male juvenile Wistar rats is greater than 14,008 mg/kg body weight.
Reliability:	score = 2, valid with restrictions
Reference:	Myers, R.C. 1976. Union Carbide Corporation (unpublished report), Butyl Propionate, Range Finding Toxicity Studies. Bushy Run Research Center, Project Report 39-93, July 9, 1976.

5.1.2 ACUTE INHALATION TOXICITY

(a)

Preferred value	reliability score = 2, valid with restrictions
Type:	other
Species:	rat/Sprague-Dawley
Exposure Time:	6 hours
Value:	substantially saturated vapor killed 0 of 5 males and 0 of 5 females
Method:	Male and female Sprague-Dawley rats, weighing between 200 and 300 g, were exposed to substantially saturated n-butyl propionate vapor for 6 hours. Vapor was generated by enclosing approximately 100 g of the test material in a sealed 100 to 151 liter chamber for 18 hours (static conditions) at 25 degree C. A mixing fan periodically agitated the chamber atmosphere to aid in distribution of the vapor. Oxygen was added, as needed, for static exposures to maintain a chamber oxygen concentration of approximately 20%. Five males and 5 females were included in each exposure regimen. Animals were weighed prior to

		exposure, and again on day 7 and day 14 prior to sacrifice. Animals were observed for signs of toxicity during and immediately following exposure, and throughout the 14-day post-exposure observation interval. A gross pathology exam was conducted on animals found dead or at sacrifice.
	Year:	1976
	GLP:	no
	Test substance:	n-butyl propionate, >99% purity
	Remarks:	Five male and five female rats were exposed to substantially saturated vapours for a 6-hour period. There was no mortality and no signs of toxicity. Rats gained weight and appeared normal throughout the 14-day post-exposure observation interval. At necropsy, all animals had no remarkable gross lesions.
	Result:	There was no mortality or signs of toxicity in male and female rats exposed to substantially saturated vapor for 6 hours.
	Comment:	The actual concentration of test material present during the exposure interval was not measured. Based on the vapor pressure of n-butyl propionate (2.86 mm Hg), the maximum concentration within the test chamber was less than 3800 ppm.
	Reliability:	score = 2, valid with restrictions
	Reference:	Myers, R.C. 1988. Union Carbide Corporation (unpublished report), UCAR® n-Butyl Propionate, Acute Toxicity and Primary Irritancy Studies. Bushy Run Research Center, Project Report 51-68, July 27, 1988.
(b)	Type:	other
	Species:	rat
	Exposure Time:	8 hours
	Value:	substantially saturated vapor killed 0 of 6 males
	Method:	Male albino rats, were exposed to dynamically generated, substantially saturated n-butyl propionate vapor for 8 hours. Vapor was generated at 21 degree C in a gas washing bottle by passing dried air at 2.5 liter/min through a fritted glass disc immersed to a depth of at least 1.5 inches in the test material. The dynamically-generated vapor was delivered to rats in an inhalation chamber maintained at 25 degree C. Animals were weighed prior to exposure, and again on day 7 and day 14 prior to sacrifice. Animals were observed for signs of toxicity during and immediately following exposure, and throughout the 14-day post-exposure observation interval. A gross pathology exam was conducted on animals found dead or at sacrifice.
	Year:	1976
	GLP:	no
	Test substance:	n-butyl propionate, purity not specified
	Remarks:	Six male rats were exposed to dynamically generated, substantially saturated vapor for an 8-hour period. There was no mortality. Signs of toxicity included poor coordination within 80 minutes and anaesthesia within 160 minutes. Rats gained weight

and appeared normal throughout the post-exposure observation interval. At necropsy, all animals had no remarkable gross lesions.

Result:	There was no mortality in male rats exposed to substantially saturated vapor for 8 hours. All animals displayed poor coordination and anaesthesia.
Reliability:	score = 2, valid with restrictions
Reference:	Myers, R.C. 1976. Union Carbide Corporation (unpublished report), Butyl Propionate, Range Finding Toxicity Studies. Bushy Run Research Center, Project Report 39-93, July 9, 1976.

5.1.3 ACUTE DERMAL TOXICITY

(a)

Preferred value	reliability score = 1, valid without restrictions; comparable to guideline study
Type:	LD50
Species:	rabbit/New Zealand White
Value:	>16 ml/kg (14,008 mg/kg)
Method:	A group of 5 male and 5 female New Zealand White rabbits (2-3 kg) received dermal administration of 16.0 ml/kg (14008 mg/kg) of undiluted n-butyl propionate for 24 hours under occluded conditions on the clipped, intact skin of the trunk. Because of the volume of test material, gauze was wrapped around the trunk over the sample to prevent leakage. The gauze was covered with impervious sheeting and wrapped with bandaging tape. Animals were returned to their cages for the 24-hr contact period. After the exposure period ended, excess material was removed to prevent oral ingestion. Skin reactions and clinical signs were observed at one hour post-dosing, and 7 and 14 days post-dosing. Animal weights were recorded at day 0, 7, and 14 days. All surviving rabbits were sacrificed at day 14. A gross pathology exam was conducted on animals found dead or at sacrifice.
Year	1988
GLP:	no
Test substance:	n-butyl propionate, >99% purity
Remark:	None of the 5 male or 5 female rabbits died after 24 hr dermal exposure to 16 ml/kg (14,008 mg/kg) n-butyl propionate. One male rabbit injured a limb and was sacrificed at 7 days for humane reasons. Local dermal effects at the application site included edema, necrosis, desquamation, fissuring, ulceration, scabs and alopecia. Diarrhea was observed in one female at 7 days, with recovery by 14 days. All animals gained weight during the 14-day observation interval. Gross pathological findings were unremarkable, with the exception of a pitted surface of the kidney in one male and dark red lungs in one female.
Result:	There was no mortality or signs of systemic toxicity in male and female rabbits after dermal exposure to 16 ml/kg (14,008 mg/kg) n-butyl propionate for 24 hours.

	Reference:	Myers, R.C. 1988. Union Carbide Corporation (unpublished report), UCAR® n-Butyl Propionate, Acute Toxicity and Primary Irritancy Studies. Bushy Run Research Center, Project Report 51-68, July 27, 1988.
(b)	Type:	LD50
	Species:	rat/Fischer 344
	Value:	>2000 mg/kg
	Method:	OECD Test Guideline No. 402 A group of 5 female Fischer 344 (8-9 weeks old) received dermal administration of 2000 mg/kg for 24 hours under occluded conditions on the clipped, intact skin of the trunk. Animals were weighed and a single dose of the test material applied to the dorsal skin. The test material was applied undiluted at a dose volume of 2.29 ml/kg (density = 0.875 g/ml). The test material was held in place with a lint dressing covered with waterproof adhesive tape. Rats were then individually housed during the contact interval. After the exposure period ended, the dressings were removed, the skin washed with warm dilute detergent solution, and dried. Clinical examination was performed three times daily for the first three days and once daily thereafter for the remainder of the 14-day observation interval. Initial (Day 1), Day 7 and Day 14 body weights were recorded and changes in body weights calculated.
	Year	1983
	GLP:	no
	Test substance:	n-butyl propionate, 99.825%
	Remark:	There was no mortality in 5 male and 5 female rats that received a single 24-hr occluded dermal application of n-butyl propionate at 2000 mg/kg. There were no signs of systemic toxicity. Application sites showed sores by Day 2 and Day 3; skin appeared normal on all animals by Day 4. All rats gained weight by the end of the observation interval. The study was terminated on Day 14.
	Result:	There was no mortality or signs of systemic toxicity in male and female rats after dermal exposure to 2000 mg/kg n-butyl propionate for 24 hours.
	Reliability:	score = 1; OECD guideline study
	Reference:	Gardner, J.R. 1989. Shell Chemical Company, London, (unpublished report), N-Butyl Propionate: Acute Oral and Dermal Toxicology, Skin and Eye Irritancy and Skin Sensitising Potential. Sittingbourne Research Center Laboratory Number SBGR 88.195, March 13, 1989.
(c)	Type:	LD50
	Species:	rabbit (male)
	Value:	>16 ml/kg (14,008 mg/kg)
	Method:	A group of 6 male albino rabbits (3-5 months old) received dermal administration of 16 ml/kg (14,008 mg/kg) of n-butyl propionate

	for 24 hours under occluded conditions on the clipped, intact skin of the trunk. Animals were immobilized during the 24-hr exposure period. Animals were observed for skin reactions and signs of toxicity during a 14-day post-exposure observation interval. All surviving rabbits were sacrificed at day 14. A gross pathology exam was conducted on animals found dead or at sacrifice.
Year	1976
GLP:	no
Test substance:	n-butyl propionate
Remark:	One of 6 male rabbits died after 24-hr dermal exposure to 16 ml/kg (14,008 mg/kg) n-butyl propionate. There were no signs systemic toxicity observed in any rabbits. Skin reaction at the application site included erythema, edema, ecchymosis at 24 hours; desquamation was observed at 14 days. At necropsy, congested lungs and kidneys and a mottled liver was noted in the animal dying on Day 1. There were no gross lesions noted in surviving animals sacrificed on Day 14.
Result:	The dermal LD50 for n-butyl propionate in male albino rabbits is > 16 ml/kg (14,008 mg/kg).
Reliability:	score = 2, valid with restrictions
Reference:	Myers, R.C. 1976. Union Carbide Corporation (unpublished report), Butyl Propionate, Range Finding Toxicity Studies. Bushy Run Research Center, Project Report 39-93, July 9, 1976.

5.1.4 ACUTE TOXICITY, OTHER ROUTES OF ADMINISTRATION

(a)

Type:	
Species:	
Value:	
Method other:	
Year:	
GLP:	
Remarks:	No data available

5.2 CORROSIVENESS/IRRITATION

5.2.1 SKIN IRRITATION/CORROSION

(a)

Preferred value	reliability score = 1, valid without restriction; comparable to guideline study
Species:	New Zealand White rabbits
Result:	no irritation
Classification:	
Method other:	Three male and three female New Zealand White rabbits were treated with 0.5 ml of n-butyl propionate for a 4-hour period. The dosage was applied to the clipped, intact skin under a gauze patch and was loosely covered with impervious sheeting. The animals

		were restrained for the 4-hour exposure period. Excess liquid was removed at the end of the exposure period. Skin reactions were scored by the Draize method at one hour and at 1, 2, 3, 7, 10 and 14 days after exposure.
	Year:	1988
	GLP:	no
	Test substance:	n-butyl propionate, >99% purity
	Remark:	When applied to the skin of six rabbits, under semi-occluded conditions for a period of 4 hours, 0.5 ml of n-butyl propionate produced no erythema, edema, or other signs of irritation on any of 6 rabbits through 7 days. Because of the lack of irritation, the study was terminated at after 7 days.
	Reference:	Myers, R.C. 1988. Union Carbide Corporation (unpublished report), UCAR® n-Butyl Propionate, Acute Toxicity and Primary Irritancy Studies. Bushy Run Research Center, Project Report 51-68, July 27, 1988.
(b)	Species:	rabbit/New Zealand White
	Result:	very slightly irritating
	Classification:	
	Method other:	OECD Test Guideline No. 404. Four rabbits (2 male, 2 female) were treated with 0.5 ml undiluted n-butyl propionate for a 4-hour period under semi-occluded conditons. The dosage was to a 6 cm x 6 cm lint patch which was then applied to the clipped, intact dorsal skin. The patch was covered with gauze and held in place by a semi-occlusive elastic adhesive bandage. After the 4-hr exposure the dressings were removed, the skin washed with water and dried. Animals were examined for erythema, edema, and other evidence of irritation or skin lesions. Erythema and edema were scored on a four point scale. The mean scores for each time point and group mean scores at 24, 48, and 72 hours and 7 days were calculated.
	Year:	1989
	GLP:	no
	Test substance:	n-butyl propionate, purity 99.825%
	Remark:	When applied to the skin of four rabbit for a period of 4 hours, 0.5 ml of n-butyl propionate produced very slight erythema. One rabbit displayed well-defined erythema at 48 and 72 hours. Group mean scores for erythema at 24, 48, and 72 hours were 1.0, 1.3, and 1.0, respectively. No edema was noted at any time. There was no evidence of irritation observed at 7 days. These data indicate that under non-occluded conditions, skin exposure to n-butyl propionate may produce a very slight local irritation of the skin.
	Reliability:	score = 1, valid without restriction; OECD guideline study
	Reference:	Gardner, J.R. 1989. Shell Chemical Company, London, (unpublished report), N-Butyl Propionate: Acute Oral and Dermal Toxicology, Skin and Eye Irritancy and Skin Sensitising

Potential. Sittingbourne Research Center Laboratory Number SBGR 88.195, March 13, 1989.

(c)	Species:	rabbit
	Result:	very slightly irritating
	Classification:	
	Method other:	Six albino rabbits (3 male, 3 female) were treated with 0.01 ml undiluted n-butyl propionate for a 24-hour period. The dosage was applied to the clipped, intact skin of the rabbit belly and left uncovered. Skin reactions were scored by the Draize method at the end of the 24-hour exposure interval.
	Year:	1976
	GLP:	no
	Test substance:	n-butyl propionate
	Remark:	When applied to the skin of six rabbit for a period of 24 hours, 0.01 ml of n-butyl propionate produced moderate capillary injection (Grade 2 on a Draize scale of 0 to 10). These data indicate that under non-occluded conditions, skin exposure to n-butyl propionate may produce a very slight local irritation of the skin.
	Reliability:	score = 2, valid with restrictions
	Reference:	Myers, R.C. 1976. Union Carbide Corporation (unpublished report), Butyl Propionate, Range Finding Toxicity Studies. Bushy Run Research Center, Project Report 39-93, July 9, 1976.
(d)	Species:	guinea pig/albino Dunkin Hartley
	Result:	slightly irritating
	Classification:	
	Method:	Groups of 4 guinea pigs (2 male, 2 female) were used in range-finding tests to determine the concentration of the test material to be used for topical induction and topical challenge for the guinea pig maximization test. Groups received topical applications of 0.3 ml of n-butyl propionate at concentrations of 25%, 50%, 75%, or 100% (m/v) in corn oil. A corn oil control group was run concurrently with the test material. Dermal test sites were evaluated for irritation on the day after administration.
	Year:	1988
	GLP:	no
	Test substance:	n-butyl propionate, purity 99.825%
	Results:	25% (m/v) in corn oil: no skin effects 50% (m/v) in corn oil: slight erythema in 1 of 4 animals 75% (m/v) in corn oil: slight erythema in 3 of 4 animals 100% (m/v) in corn oil: slight erythema in 4 of 4 animals
	Remark:	A deficiency of this study is that a concurrent positive control group was not run along with the test material, vehicle, and negative control groups.
	Reliability:	score = 2, valid with restriction

	Reference:	Gardner, J.R. 1989. Shell Chemical Company, London (unpublished report), N-Butyl Propionate: Acute Oral and Dermal Toxicology, Skin and Eye Irritancy and Skin Sensitising Potential. Document Number SBGR 88.195, March 13, 1989.

5.2.2 EYE IRRITATION/CORROSION

(a)	Preferred value	reliability score = 1, valid without restrictions; comparable to guideline study
	Species:	rabbit/New Zealand White
	Result:	moderately irritating
	Classification:	
	Method:	A group of 6 New Zealand White rabbits (4 male, 2 female) were dosed with volumes of 0.1 ml undiluted n-butyl propionate. The dose was instilled into the lower conjunctival sac of one eye per animal. The eyelids were held together for one second to prevent loss of the test material. Six eyes were dosed. The eyes were scored by the Draize method at one and four hours, and 1, 2, 3, and 7 days after dosing. Fluorescein (2%) staining was used to determine corneal injury before dosing and at readings 1 day after dosing.
	Year:	1988
	GLP:	no
	Test substance:	n-butyl propionate, >99% purity
	Remark	Instillation of 0.1 ml of primary amyl acetate did not cause corneal injury in any of six animals. Transient iritis was apparent in 2 eyes. Minor to moderate conjunctival irritation developed in 6 eyes within one hour. A substantial discharge was noted in each eye. After 24 hours, only minor (Draize score=1) conjunctival redness remained in all rabbits. By 48 hours, 5 of 6 eyes appeared normal; one eye had minor conjunctival redness. All six eyes were normal after 72 hours.
	Reference:	Myers, R.C. 1988. Union Carbide Corporation (unpublished report), UCAR® n-Butyl Propionate, Acute Toxicity and Primary Irritancy Studies. Bushy Run Research Center, Project Report 51-68, July 27, 1988.
(b)	Species:	rabbit/New Zealand White
	Result:	moderate irritation
	Classification:	
	Method	OECD Test Guideline No. 405 A group of 4 rabbits were dosed with volumes of 0.1 ml undiluted n-butyl propionate. The dose was instilled into the lower conjunctival sac of the rabbit eye. The treated eye was gently held closed for a few seconds to prevent loss of the test material. The eye was not irrigated. The immediate reaction of each rabbit was scored as an initial pain response using a six-point

	scale. Ocular reactions to treatment were noted and scored using standard grades (Draize) at 24, 48, and 72 hours, and again at 7 days.
Year:	1989
GLP:	no
Test substance:	n-butyl propionate, purity 99.825%
Remark	Instillation of 0.1 ml undiluted n-butyl propionate into the eyes of four rabbits (2 male, 2 female) resulted in moderate initial pain response. There was no evidence of chemosis, corneal injury, or irititis. All rabbits displayed mild to moderate conjunctival erythema with slight ocular discharge within one hour after instillation, which persisted for 24 hours. Although mild (Grade 1) erythema remained at 48 hr, only one animal displayed a slight ocular discharge. Slight conjunctival erythema persisted for 72 hours. All eyes were normal by day 7.
Reliability:	score = 1; valid without restriction; OECD guideline study.
Reference:	Gardner, J.R. 1989. Shell Chemical Company, London, (unpublished report), N-Butyl Propionate: Acute Oral and Dermal Toxicology, Skin and Eye Irritancy and Skin Sensitising Potential. Sittingbourne Research Center Laboratory Number SBGR 88.195, March 13, 1989.

5.3 SKIN SENSITISATION

(a)

Preferred value	reliability score = 2, valid with restriction
Type:	Guinea pig maximization test
Species:	Dunkin Hartley albino guinea pigs
Result:	negative
Classification:	
Method:	OECD Test Guideline No. 406 Procedures used were based on the methods described in Magnusson and Kligman, 1969. The identification of contact allergens by animal assay. The guinea pig maximization test. J. Investigative Dermatology 52: 268-276. Groups of 4 guinea pigs (2 male, 2 female) were used in range-finding tests to determine the concentration of the test material to be used for intradermal induction, topical induction and topical challenge for the main test. Groups received 0.1 ml doses by intradermal injections of butyl propionate at concentrations of 0.05, 0.1, 0.5 and 1.0% (m/v) in corn oil. Animals were examined the following day to determine the maximum concentration that could be used in the main test without causing untoward toxicity. Additional groups received topical applications of 0.3 ml of n-butyl propionate in corn oil at concentrations of 25, 50, 75, and 100%. Dermal test sites were evaluated for irritation on the day after administration. The concentration selected for topical induction was that which just caused irritation, and the

concentration tested for topical challenge was that which was just non-irritating. Based on range-finding results, the following concentrations of butyl propionate were selected:

Intradermal induction:	0.5% (m/v) in corn oil and/or Freunds Complete Adjuvant (FCA)
Topical induction:	50% (m/v) in corn oil
Topical challenge:	50% (m/v) in corn oil

The main test was conducted using a group of 10 male and 10 female guinea pigs with a control group of 5 males and 5 females. Body weights were recorded at the beginning and end of the main study.
Induction: Animals were shaved in the shoulder region and two row of intradermal injections were made, one on either side of the midline:

Anterior:	0.1 ml FCA
Middle:	0.1 ml n-butyl propionate in corn oil
Posterior:	0.1 ml n-butyl propionate in 50:50 FCA/corn oil

Control animals were similarly treated but did not receive the test material. One week after induction by intradermal injection, the same area of the dorsal skin was shaved; a 16cm x 16 cm patch of filter paper was moistened with 0.3 ml of a 50% solution of n-butyl propionate in corn oil and placed over the sites of the intradermal injections. The patches were covered with occlusive tape and held in place by elastic adhesive bandage for 48 hours. Similar patches were prepared with corn oil alone and were applied to control animals.
Challenge: Three weeks after the intradermal phase of induction, hair was shaved from one flank of all test and control animals. A 4 cm x 4 cm patch of filter paper was moistened with 0.1 ml of a 50% solution of n-butyl propionate in corn oil and placed on the shaved area. The patch was held in place by an elastic adhesive bandage. Control animals were treated with the same formulation of the test material that was applied to the test group. After 24 hours, the patches were removed and the challenge sites examined for evidence of response and scored on a 4-point scale (0 = no response through 3 = maximum response) for erythema and edema. The results of the test is expressed as the number of positive responses (scores >0) shown by the test animals at 24 and 48 hours after removal of the challenge patches.

Year:	1988
GLP:	no
Test substance:	n-butyl propionate, purity 99.825%
Results:	None of the 20 test animals displayed any positive reaction at either 24 or 48 hours after removal of the challenge patches.

	Under conditions of this study, n-butyl propionate exhibited no potential to produce dermal sensitisation in guinea pigs.
Remark:	A deficiency of this study is that a concurrent positive control group was not run along with the test material, vehicle, and negative control groups.
Reference:	Gardner, J.R. 1989. Shell Chemical Company, London (unpublished report), N-Butyl Propionate: Acute Oral and Dermal Toxicology, Skin and Eye Irritancy and Skin Sensitising Potential. Document Number SBGR 88.195, March 13, 1989.

5.4 REPEATED DOSE TOXICITY

(a)

Preferred value	reliability score = 1, valid without restrictions; guideline study
Species:	rat
Strain:	Sprague-Dawley
Sex:	male and female
Route of Admin:	inhalation
Exposure Period:	13 weeks
Freq. of Treatment:	6 hours/day, 5 days/week
Post Exposure Observation Period:	8 weeks
Doses:	0, 250, 750, 1500 ppm
Control Group:	yes
NOEL:	250 ppm
LOEL:	750 ppm
Method:	USEPA TSCA Health Effects Test Guidelines for Subchronic Exposure Inhalation Toxicity (40 CFR 54, Guideline 798.4900, May 16, 1989). Groups of 15 male and 15 female Sprague-Dawley rats (approximately 7 weeks old, 222-255 g for males, 151-183 g for females) were assigned to 4 groups and exposed to n-butyl propionate at target concentrations of 0, 250, 750, or 1500 ppm for 6 hours per day, 5 days per week, for 13 consecutive weeks for a minimum of 65 total exposures. Following 13 weeks of exposure, 5 rats per sex per group were arbitrarily selected for an approximate 8-week (non-exposure) recovery period. Rats were housed individually in wire-mesh cages. All animals were housed separately by test group. During exposures, animals were housed in stainless steel wire-mesh cages; food and water was withheld during exposure. Animals were exposed in four 1-cubic meter glass and stainless steel whole-body inhalation chambers operated under dynamic conditions with airflows of at least 12-15 changes per hour, ensuring a minimum oxygen content of 19%. One chamber was designated for each exposure group. The control group was exposed to clean, filtered air under conditions identical to the test groups. All rats were exposed simultaneously in the four exposure chambers at approximately the same time each day. Chamber temperature and humidity was

monitored continuously and recorded every 35 minutes. Measured daily mean temperatures ranged from 22 degree C to 28 degree C (71 to 82 degree F) and daily mean relative humidity ranged from 34 % to 63%. Animals were rotated on a daily bases through various cage positions to compensate for possible variations in exposure concentrations. Vapor was generated by metering the liquid n-butyl propionate from a piston pump onto 8- and 12- mm glass beads within a glass vaporization column wrapped with flexible electric heating tape. Vaporization temperature was controlled by a model CN370 digital temperature controller (Omega Engineering). Compressed air for vaporization was metered into the vaporization column below the glass beads. The vapor was piped to the chamber inlet where the concentration was reduced to desired levels by mixing with chamber ventilation air. Actual chamber concentrations were analyzed at approximate 35 minute intervals during exposure using a HP 5890 Series II gas chromatograph equipped with a flame ionization detector. Average measured chamber concentrations were within 1 to 2% of the target concentrations. All rats were observed twice daily for morbidity and mortality. A clinical examination was performed on all animals prior to each exposure. Animals were observed for clinical signs during exposure and approximately one hour after completion of exposure. On non-exposure days, including the recovery period, clinical examinations were performed each day. Detailed physical examinations were conducted weekly, beginning one week prior to initiation of exposure, and just prior to scheduled sacrifice. Body weights of all animals were recorded weekly, beginning one week prior to exposure, and just prior to sacrifice. Mean body weights and body weight changes were calculated for each interval. Individual food consumption was recorded weekly for all animals, beginning one week prior to exposure. Ocular examinations were conducted on all rats prior to initiation of exposure, and during study week 12. All ocular examinations were conducted using an indirect ophthalmoscope and/or slit lamp or other equivalent equipment, and performed by a veterinary ophthalmologist. Blood samples from a lateral tail was collected for clinical pathology evaluations from all animals during study week 4 and from all animals designated for study week 13 necropsy; blood was collected from the vena cava during sacrifice by exsanguination. Gross examinations were performed and all major organs and tissues, including the nasal cavity, were saved. The adrenals, brain, kidneys, liver, lungs, ovaries (females only), and testes (males only) from all animals were weighed. Microscopic tissue evaluations were performed on all tissues from animals in the control and 1500 ppm group. Microscopic examination of the nasal cavities was performed on

all animals. Six cross sections were prepared for microscopic examination according to a method described by Morgan (Morgan, R.T. 1991. Toxicological Pathology 19: 337-351).

Year: 1997

GLP: yes

Test substance: n-butyl propionate, purity 99.61%

Remark: Repeated exposure to n-butyl propionate at concentrations up to 1500 ppm produced few adverse effects in young adult male and female rats. No systemic target organ effects were noted. The only systemic effects detected were reductions relative to controls in body weights, body weight gains, and feed consumption rates. These effects were found to be reversible, and normal values for these parameters were achieved after exposure had ceased. The most pronounced effect associated with exposure to n-butyl propionate vapor was an apparent local effect to the nasal cavity. A concentration-dependent increased incidence and severity of degeneration of the olfactory epithelium was observed at 750 and 1500 ppm. These changes were reversible. An evaluation of the nasal cavities of rats after an 8-week recovery interval found no further degenerative changes; there was also evidence of substantial olfactory epithelium repair. At 250 ppm, there were no observable effects on the olfactory epithelium. The NOEL for n-butyl propionate was determined to be 250 ppm, based on the degeneration of olfactory epithelium.

Results: There was one male in the 250 ppm group found dead on exposure Day 41; necropsy revealed the cause of death was marked upper and lower urinary tract infection which was not considered to be test article-related. All other animals survived to scheduled necropsy. No exposure-related clinical signs were observed in during exposure or recovery periods. Other findings were seen infrequently in single animals and at similar incidences in control and treated groups. Mean body weights were decreased throughout the exposure interval when compared to controls; mean body weight and body weight gains in the 1500 ppm males were reduced by 10% and 20%, respectively, when compared to control males. During the recovery period, mean body weights and body weight gains were similar to control values; by the end of the recovery period, mean body weight in the 1500 ppm males was within 1% of the control group value. The 1500 ppm group females experienced slight, transient decreases in mean body weight during study weeks 0-1 and 2-3; no other adverse effects were observed on body weight data in the 1500 ppm female group. No body weight trends were apparent in the 250 and 750 ppm groups. Weekly food consumption was reduced for males in the 1500 ppm group throughout the exposure period; consumption was decreased by 15% when compared to controls at study week 12-13. Food

consumption for 1500 ppm recovery group males was similar to control group values during the recovery interval. There were no exposure-related effects on food consumption in the 1500 ppm females or the 250 ppm and 750 ppm male or female rats. No consistent pattern of exposure-related changes were observed for hematology or clinical chemistry parameters. A decrease in mean corpuscular hemoglobin (MHC) was observed in females from the 750 ppm and 1500 ppm groups at week 4, and an increase in MCH was noted in males from the 750 ppm group at week 13. Females in the 750 ppm group displayed increased prothrombin tine at week 13. Sporadic decreases in serum enzyme concentrations were noted during clinical chemistry evaluations. These included decreases in week 4 evaluations in aspartate aminotransferase in 1500 ppm males and gamma glutamyltransferase in 1500 ppm females, and increases in week 13 in phosphorus in 750 ppm females and potassium in 1500 ppm females. Ophthalmologic examination at the end of the exposure and recovery period revealed no ocular abnormalities related to exposure to n-butyl propionate. At necropsy, there were some differences noted for organ weights when compared to controls. Overall organ weight data, however, indicate that these changes were not exposure-related. At study week 13, 1500 ppm males had a decreased absolute liver weight and increased mean brain and testes weights relative to final body weight. These changes were considered secondary to the reduced final body weight mean in this group. Similar findings were not observed in 1500 ppm females. Among recovery group males sacrificed after 8 weeks, no differences in organ weights were observed relative to controls. There were no macroscopic lesions observed at necropsy that could be ascribed to n-butyl propionate exposure. Upon microscopic evaluation of tissues, the only exposure-related findings were limited to the nasal cavity of rats in the 750 ppm and 1500 ppm groups. Rats in the 750 ppm and 1500 ppm groups sacrificed at the end of the 13-week exposure interval exhibited degenerative changes to the nasal cavity olfactory epithelium that consisted of cytoplasmic vacuolation and necrosis. Vacuoles were present at different heights within the olfactory mucosa and often contained degenerative or necrotic cells. Necrosis of the olfactory epithelium was characterized by pyknotic or fragmented nuclei and brightly stained acidophic cytoplasm. Atrophy of the olfactory epithelium was characterized by a mucosa of decreased height and populated by a reduced number of cells. These olfactory epithelial changes were noted in nasal sections taken at levels 3,4,5, and 6. Degenerative changes, however, were most pronounced and consistently present at levels 3 and 4. The affected areas consisted of a relatively small portions of the overall olfactory mucosal surface. There was no evidence of

exposure-related effects on the olfactory epithelium in rats exposed to 250 ppm. Microscopic examination of tissues from recovery group animals indicated that substantial to complete recovery of the olfactory epithelium occurred during the 8 weeks following the last exposure. Olfactory epithelia in the treated groups displayed normal height and cellularity; minimal evidence of necrosis of the olfactory epithelium was noted in 4 of 10 animals in the 1500 ppm group.

Reference:

1) Ulrich, C.E. 1997. A 13-Week Inhalation Toxicity Study of n-Butyl Propionate in Albino Rats. WIL Research Laboratories, Inc., Ashland, OH. Unpublished study dated April 28, 1997.
2) Banton, M.I., Tyler, T.R., Ulrich, C.E., Nemec, M.D., and Garman, R.H. 2000. Subchronic and developmental toxicity studies of n-butyl propionate vapor in rats. J. Toxicol. Environ. Health 61: 79-105.
3) Hardisty, J.F., Harkema, J.R., Lomax, LG., Morgan, K.T., and Garman, R.H. 1999. Pathology Advisory Group Review of the Nasal Histopathology of the Nasal Olfactory Mucosa from Selected Inhalation Toxicity Studies Conducted with Volatile Chemicals. Experimental Pathology Laboratories, Inc., Research Triangle Park, NC. Unpublished report dated February 22, 1999.
4) Hardisty, J.F., Garman, R.H., Harkema, J.R., Lomax, LG., and Morgan, K.T. 1999. Histopathology of nasal olfactory epithelium from selected inhalation toxicity studies conducted with volatile chemicals. Toxicol. Pathol. 6: 618-627.

(b)

Species:	rat
Strain:	Sprague-Dawley
Sex:	male and female
Route of Admin:	inhalation
Exposure Period:	2 weeks
Freq. of Treatment:	6 h/day, 5 days/week for a total of 10 exposures
Post Exposure Observation Period:	none
Doses:	0, 250, 500, 2500, or 4000 ppm
Control Group:	yes
NOEL:	500 ppm
LOEL:	2500 ppm

Method: Male and female Sprague-Dawley rats (225-256 g for males, 152-190 g for females) were assigned to 5 groups, 5 per sex, and exposed to n-butyl propionate at target concentrations of 0, 250, 500, 2500, or 4000 ppm for 2 weeks, 6 hours per day, 5 days per week, for two consecutive weeks for a total of 10 exposures. Rats were housed individually in wire-mesh cages. All animals were housed separately by test group. During exposures, animals were housed in stainless steel wire-mesh cages; food and water was withheld during exposure. Animals were exposed in five 1 cubic meter glass and stainless steel whole-body inhalation

chambers operated under dynamic conditions with airflows of at least 12-15 changes per hour, ensuring a minimum oxygen content of 19%. One chamber was designated for each exposure group. The control group was exposed to clean, filtered air under conditions identical to the test groups. All rats were exposed at approximately the same time each day. Chamber temperature and humidity was monitored continuously and recorded every 35 minutes. Measured daily mean temperatures ranged from 20 degree C to 24 degree C (68 to 75 degree F) and daily mean relative humidity ranged from 23 % to 47%. Animals were rotated on a daily bases through various cage positions to compensate for possible variations in exposure concentrations. n-Butyl propionate vapor was generated by metering the liquid material from a piston pump onto 8- and 12- mm glass beads within a glass vaporization column wrapped with a flexible electric heating tape. Vaporization temperature was controlled by a model CN370 digital temperature controller (Omega Engineering). Compressed air for vaporization was metered into the vaporization column below the glass beads. The vapor was piped to the chamber inlet where the concentration was reduced to desired levels by mixing with chamber ventilation air. Actual chamber concentrations were analyzed at approximate 35 minute intervals during exposure using a HP 5890 Series II gas chromatograph equipped with a flame ionization detector. Average measured chamber concentrations were within 2 to 5% of the target concentrations. All rats were observed twice daily for morbidity and mortality. Animals were observed for clinical signs during exposure and approximately one hour after completion of exposure. Body weights of all animals were recorded twice weekly, beginning one week prior to exposure, and prior to sacrifice. Mean body weights and body weight changes were calculated for each interval. Individual food consumption was recorded weekly for all animals, beginning one week prior to exposure. All rats were sacrificed on the day following the final exposure. Gross examinations were performed and selected tissues, including the nasal cavity, were saved; the adrenals, brain, kidneys, liver, lungs, ovaries (females only), and testes (males only) from all animals were weighed. Microscopic examination of the nasal cavities was performed on all animals. Six cross sections were prepared for microscopic examination according to a method described by Morgan (Morgan, R.T. 1991. Toxicological Pathology 19: 337-351).

Year:	1996
GLP:	yes
Test substance:	n-butyl propionate, purity 99.1%
Results:	There was no mortality in any group. Exposure-related clinical signs observed in males and females in the 2500 and 4000 ppm groups included drooping or half-closed eyelids and salivation

during exposure, and dried brown or red material or staining around the mouth and/or nose, noted one hour following exposure. Increased incidences of lacrimation were noted in males in the 4000 ppm group during exposure, and increased incidences of yellow or tan staining in the urogenital or ventral body surfaces was noted in females in the 4000 ppm group. Mean body weight gains were unaffected by exposure with the exception of reduced body weight gains for both sexes in the 4000 ppm group during study days 0-3. Weekly food consumption was reduced for both sexes in the 2500 and 4000 ppm groups during week 1; food consumption remained reduced relative to the control group in females in the 4000 ppm group. No exposure-related internal findings were observed at scheduled necropsy. No effects of exposure were observed on organ weights (absolute and relative to final body weight). Exposure-related lesions consisting of cytoplasmic vacuolation, necrosis, and/or atrophy of the olfactory epithelium, with or without dilation of Bowman's glands, were noted in males and females in the 2500 and 4000 ppm groups. These lesions were multifocal, generally bilateral, and confined to nasal sections III, IV, V, and VI. No treatment-related microscopic lesions were observed in males or females in the 250 or 500 ppm groups.

Reliability: score = 1, valid without restrictions

Reference: Nemec, M.D. 1996. A Combined 2-Week Range-Finding Inhalation Toxicity and Developmental Toxicity Study of n-Butyl Propionate in Rats. WIL Research Laboratories, Inc., Ashland, OH. Unpublished study dated November 14, 1996.

(c)

Species:	rat
Strain:	Fischer 344
Sex:	male and female
Route of Admin:	inhalation
Exposure Period:	11 days
Freq. of Treatment:	6 hours/day, 5 days a week for a total of 9 exposures
Post Exposure Observation Period:	26 days
Doses:	0, 800, 2600, 3200 ppm
Control Group:	yes
NOAEL:	
LOEL:	800 ppm
Method:	Equivalent to OECD 413

Male and female 344 rats were assigned to 4 groups, 10 per sex per group, and exposed to n-butyl propionate at target concentrations of 0, 800, 2600, 3200 ppm for 6 hours per day, 5 days per week, for a total of 9 exposures. An additional 10 animals per sex were included in the control and high dose (3200 ppm) groups. After the final exposure, 10 rats per sex from each group were sacrificed; the remaining animals in the

control and high 3200 ppm groups (recovery group, 10 rats per sex per group) were held for a 26-day observation period and then sacrificed. Rats were approximately 55 days old at initiation of exposure. Animals were housed individually stainless steel wire-mesh cages. All rats were housed separately by test group. Food and water was withheld during exposure but available *ad libitum* at all other times. Animals were exposed in 1330 L stainless steel and glass inhalation chambers for 6 hours per day. Metering of the liquid n-butyl propionate into a heat glass evaporator generated vapours of the test material. Chamber concentrations were analysed approximately twice per hour by a gas chromatograph equipped with a flame ionization detector. Average chamber concentrations were within 1 to 3% of the target concentration. Chamber temperature and humidity were monitored continuously and recorded twice per hour during exposure. Daily mean chamber values ranged from 20.2 to 24.1 degree C; daily mean chamber relative humidity ranged from 29.6 to 59.1%. During exposures, clinical observations were recorded on a group basis. Preceding and following exposures, all animals were individually observed for signs of toxicity. On non-exposure days, animals were observed once per day for overt clinical signs and twice per day for morbidity and mortality. Ophthalmic examinations were conducted prior to first exposure, and following the last exposure. Body weights of all animals were recorded prior to exposure, and on Study Days 2,5,8,9 and immediately prior to sacrifice. Body weights for animals held during the post-exposure recovery period were recorded weekly and just prior to sacrifice. Serum chemistry and haematological evaluations were performed on blood samples collected from all rats on the day of sacrifice.
Prior to the first exposure, all animals were evaluated using a functional observational battery (FOB) of screening tests designed to detect alterations in central and peripheral nervous system function. During the second week of exposure, the FOB was performed again on all animals on Thursday (males only) and Friday (females only). The FOB testing regimen was staggered over two days to accommodate the inhalation exposure schedule. Animals were tested by trained technicians who were not aware of the animals' treatment.
Ten rats per sex per exposure group were individually housed in round polycarbonate metabolism cages; food and water consumption was measured for approximately 15 hours following 9 (females) or 8 (males) exposures. Urine was collected while rats were housed in metabolism cages, food and water was available *ad libitum*. Food and water consumption was measured, and urine was collected in a similar manner over a 16-hour interval for all recovery groups rats at the end of the 26-day recovery interval. Upon sacrifice, non-fasted animals

were weighed, anaesthetised, and sacrificed by brachial artery exsanguination. A complete necropsy was performed on all animals. The liver, kidneys, brain, adrenals, lungs, spleen, and testes (males only) were weighed. Selected tissues, including the nasal turbinates, were saved; histologic examination was performed for tissues from all animals in the control and high dose groups. The nasal turbinates from all groups, including the low and intermediate dose groups, were subject to microscopic examination.

Year: 1993

GLP: yes

Test substance: n-butyl propionate, purity 99.9%

Remark: There were no treatment related changes observed in the functional observational battery (FOB) evaluations in rats exposed to n-butyl propionate vapor for 9 days over an 11-day period. Rats exposed to n-butyl propionate exhibited decreased body weight and body weight gain, decreased food and water consumption, and microscopic changes in the anterior olfactory mucosa. These changes were observed at all concentrations tested. Thus., a no-observed-effect-level (NOEL) was not determined. The LOEL for this study was 800 ppm.

Result: No mortality occurred during the study. No exposure-related clinical signs were observed in any group exposed to n-butyl propionate. There were no treatment related changes observed in the functional observational battery (FOB) evaluations in rats exposed to n-butyl propionate. Decreases in body weight and/or body weight gain were observed for males and females for all exposure groups. Exposure-related decreases in food consumption was observed for male and female rats from the 1600 and 3200 ppm groups. Decreases in water consumption were observed in females from the 1600 and 3200 ppm exposure groups. Among recovery group animals, at the end of the recovery period, mean body weights, body weight gains, and food and water consumption were comparable to controls. Various transient changes in clinical parameters were observed at the end of the exposure regimen. These changes were primarily due to body weight loss, decreased food and water consumption, and changes in water balance in the animals. Concentration-dependent decreases in urine volume and increases in urine osmolality were observed for both sexes from all exposure groups. Urine pH was decreased, and urine protein and bilirubin were elevated for 3200 ppm males. Urine pH was decreased for females from the 1600 and 3200 ppm groups. Following recovery, no differences in any urinalysis parameters were noted in male rats. In females rats, slightly increased bilirubin and urobilinogen were observed. Increases in erythrocyte count, hemoglobin, and hematocrit were noted for males and females in the 3200 ppm group; hemoglobin values

were also increased for females from the 1600 ppm group. Total leukocytes and lymphocytes were decreased for females from all exposure groups; decreases in reticulocyte counts were observed for females from all exposure groups and for males from the 1600 and 3200 ppm groups. At the end of the recovery period, male and female rats from the 3200 ppm group exhibited no differences in hematology parameters compared to control values. Decreases in alkaline phosphatase were observed for males in the 1600 and 3200 ppm groups, and decreases in calcium and phosphorus were observed for females in the 3200 ppm group. Recovery group females from the 3200 ppm group still exhibited a decrease in calcium.

Ophthalmologic examination at the end of the exposure and recovery period revealed no ocular abnormalities related to exposure to n-butyl propionate. The mean weight of the adrenals relative to body weight was increased in males and females from the 1600 and 3200 ppm groups. Absolute and relative spleen weight was reduced for females in the 1600 and 3200 ppm groups. Among all exposure group males, there was an increase in the relative weight of the testes; an increase in relative lung weight was noted for males from the 3200 ppm group. A necropsy, there were no gross lesions following exposure or the recovery period that could be attributed to n-butyl propionate exposure. Microscopic examination revealed that the only tissue affected was the olfactory epithelium in the anterior of the nasal cavity. Vacuolization of the olfactory epithelium, with occasional atrophy, was observed in rats from all exposure groups, with the incidence and severity increasing with increasing exposure concentration. Intraepithelial cysts within the olfactory mucosa were more prevalent in exposed rats than controls, with increased frequency in the 1600 and 3200 ppm groups. Atrophy and intraepithelial cysts were seen more frequently in the 3200 ppm females than the males. Lesions were not observed in any tissue sections taken from the posterior olfactory mucosa of the nasal cavity.

Vacuolization and intraepithelial cysts of the anterior portion of the olfactory epithelium were observed in the nasal cavities of males and females from the 3200 ppm group following the 26-day recovery period.

Reliability: score = 1, valid without restriction; comparable to guideline study

Reference: Werley, M.S., Chun, J.S., and Kintigh, W.J. 1993. Union Carbide Corporation (unpublished report). n-Butyl Propionate: Nine-Day Vapor Inhalation Study in Rats. Bushy Run Research Center, Project ID 91U0091, May 7, 1993.

5.5 GENETIC TOXICITY IN VITRO

A. BACTERIAL IN VITRO TEST

(a)	Preferred value	(reliability score = 2, valid with restrictions)
	Type:	Salmonella/microsome bacterial mutagenicity assay (Ames test)
	System of Testing:	*Salmonella typhimurium*, strains TA 98, TA 100, TA 1535, TA 1537, TA 1538;
	Concentration:	0, 31.25, 62.5, 125, 250, 500, 1000, 2000, 5000 ug/plate
	Metabolic Activation:	with and without
	Result:	With metabolic activation: negative Without metabolic activation: negative No evidence of mutagenicity was observed at any of the tested doses, either by evidence of a dose-response or by a 2.5-fold increase in the number of reverent colonies relative to control values. All strains exhibited a positive mutagenic response with positive controls tested both with and without metabolic activation. Negative control spontaneous reverent rates were within the historical range of the laboratory.
	Method other:	according to: Ames, B.N., McCann, J. and Yamasaki, F. 1975. Methods for detecting carcinogens and mutagens with Salmonella/mammalian-microsome mutagenicity test. Mutation Research 31: 347-364. n-Butyl propionate was dissolved in acetone; all dilutions were prepared in acetone on the day of testing. Solutions of n-butyl propionate in acetone (20 ul volumes) were added to top agar mix to give final concentrations of 31.25, 62.5, 125, 250, 500, 1000, 2000, 5000 ug/plate. All doses were tested in triplicate, in the presence and absence of metabolic activation, in 5 tester strains. The S9 microsomal fraction was obtained from liver homogenate from male Fischer 344 rats pre-treated with Arochlor 1254; a final concentration of 10% S-9 was used in all assays. Concurrent solvent (acetone) and positive controls were run concurrently with the test material. Postive controls for cultures tested without microsomal activation were sodium azide in TA1535 and TA100; 9aminoacridine in TA1537; 2-nitrofluorine in TA1538 and TA98; positive controls in cultures with microsomal activation: 3,4-benzo(a)pyrene in TA1538/98/100; 2-aminoanthracene in TA1535; neutral red in TA1527. A compound was considered a bacterial mutagen if the number of revertant colonies is at least 2.5 times the solvent control for at least one dose level or there was a reproducible dose-related increase in the number of revertant colonies.
	Year:	1988
	GLP:	yes
	Test substance:	n-butyl propionate, purity not specified
	Remark:	n-Butyl propionate did not produce a mutagenic response in any of the Salmonella tester strains, in the presence or absence of metabolic activation, up to a dose of 5000 ug/plate.

	Results:	The test material formed an oily smear on the surface of the top agar at 5000 ug/plate, indicating it was not miscible in the aqueous test system at this concentration. No residue was noted in plates at 2000 ug/plate. Microscopic evaluation of the background lawn showed no evidence of cytoxicity at doses up to 5000 ug/plate either in the presence or absence of metabolic activation. The activity of the S-9 mix and the sensitivities of the bacterial tester strains were monitored by treating cultures with known positive control compounds..
	Remark:	A deficiency of this study is that the purity of the test material was not specified.
	Reference:	Brooks, T.M. and Wiggins, D.E., 1998. Shell Chemical Company, (unpublished report), Bacterial Mutagenicity Studies with n-Butyl Propionate. Sittingbourne Research Center Laboratory Number SBGR 88.208, November 11, 1989.
(b)	Type:	Escherichia coli bacterial mutagenicity assay
	System of Testing:	*Escherichia coli*, strainWP2 uvrA pKM101
	Concentration:	0, 31.25, 62.5, 125, 250, 500, 1000, 2000, 5000 ug/plate
	Metabolic Activation:	with and without
	Result:	With metabolic activation: negative Without metabolic activation: negative No evidence of mutagenicity was observed at any of the tested doses, either by evidence of a dose-response or by a 2.5-fold increase in the number of reverent colonies relative to control values. The E.coli strain exhibited a positive mutagenic response with the positive control tested both with and without metabolic activation. Negative control spontaneous reverent rates were within the historical range of the laboratory.
	Method other:	Venitt, S. and Crofton-Sleigh, C. 1981. Mutagenicity of 42 coded compounds in a bacterial assay using Escherichia coli and Salmonella typhimurium. *In*: de Serres, F.J. and Ashby, J. Evaluation of Short-Term Tests for Carcinogens: Report of the International Program. Chapter 32, pp.351-360. Elsevier, New York. n-Butyl propionate was dissolved in acetone; all dilutions were prepared in acetone on the day of testing. Solutions of n-butyl propionate in acetone (20 ul volumes) were added to top agar mix to give final concentrations of 31.25, 62.5, 125, 250, 500, 1000, 2000, 5000 ug/plate. All doses were tested in triplicate, in the presence and absence of metabolic activation, in 5 tester strains. The S9 microsomal fraction was obtained from liver homogenate from male Fischer 344 rats pre-treated with Arochlor 1254; a final concentration of 10% S-9 was used in all assays. Concurrent solvent (acetone) and positive controls were run concurrently with the test material. The postive control for cultures tested without microsomal activation was potassium dichromate; the positive control for cultures with metabolic

	activation was 3.4-benzyo(a)pyrene. A compound was considered positive for bacterial mutagenicity if the number of revertant colonies was at least 2.5 times the solvent control for at least one dose level or there was a reproducible dose-related increase in the number of revertant colonies.
Year:	1988
GLP:	yes
Test substance:	n-butyl propionate, purity not specified
Remark:	n-Butyl propionate did not produce a mutagenic response in any of the Salmonella tester strains, in the presence or absence of metabolic activation, up to a dose of 5000 ug/plate.
Results:	The test material formed an oily smear on the surface of the top agar at 5000 ug/plate, indicating it was not miscible in the aqueous test system at this concentration. No residue was noted in plates at 2000 ug/plate. Microscopic evaluation of the background lawn showed no evidence of cytoxicity at doses up to 5000 ug/plate either in the presence or absence of metabolic activation. The activity of the S-9 mix and the sensitivities of the E. coli tester strain was monitored by treating cultures with known positive control compounds..
Remark:	A deficiency of this study is that the purity of the test material was not specified.
Reliability:	score = 2, valid with restriction
Reference:	Brooks, T.M. and Wiggins, D.E., 1998. Shell Chemical Company, (unpublished report), Bacterial Mutagenicity Studies with n-Butyl Propionate. Sittingbourne Research Center Laboratory Number SBGR 88.208, November 11, 1989.

B. NON-BACTERIAL IN VITRO TEST

(a) Preferred value reliability score = 1, valid without restrictions; guideline study

Type:	In vitro chromosomal aberration assay
System of Testing:	Rat lymphocytes
Concentration:	0, 20.3, 40.6, 81.3, 162.5, 325, 650, and 1300 ug/ml
Metabolic Activation:	with and without
Result:	With metabolic activation: negative Without metabolic activation: negative There was no increase in the incidence of chromosomal aberrations in rat lymphocyte cultures treated with butyl propionate for 4 or 24 hours either in the presence or absence of metabolic activation. Cultures treated with positive controls displayed significantly higher incidences of chromosomal aberrations in all assays. Negative control spontaneous aberration rates were within the historical range of the laboratory.
Method:	Study conducted to comply with the following guidelines OECD #473, In vitro mammalian chromosome aberration test;

USEPA Health effects testing guidelines, OPPTS 870.5375, In vitro mammalian chromosome aberration test;
EC B.10 Mutagenicity - In vitro mammalian chromosome aberration test.
n-Butyl propionate was tested in rat lymphocyte cultures at 20.3, 40.6, 81.3, 162.5, 325, 650, and 1300 ug/ml both in the presence and absence of metabolic activation. In one test, cells were exposed to butyl propionate for 4 hours and then harvested 20 hours after termination of exposure. In a second test, cells were exposed continuously to butyl propionate for 24 hours and then harvested. Butyl propionate was dissolved in DMSO and further diluted with culture medium to obtain test concentrations. Negative control cultures were exposed to 1% DMSO, positive control cultures were exposed to mitomycin C without S-9, and cyclophosphamide with S-9. All solutions were analysed by gas chromatography with flame ionisation detection to verify test concentrations.
Blood samples were collected by cardiac puncture from 17 week old male Sprague-Dawley rats. In each assay, blood samples from a minimum of two rats were polled and whole blood cultures were prepared using buffered medium supplemented with 10% fetal bovine serum. Cultures were initiated by inoculating 0.5 ml whole blood into tissue culture flasks containing 5 ml culture medium and incubating at 37 degree C for 48 hours.
Experiment 1: Approximately 48 hours after initiation of cultures, lymphocytes were collected by centrifugation and placed in 15 ml tubes. Cells were exposed to cell medium containing n-butyl propionate for 4 hours at 37 degree C. Positive and negative controls were run concurrently. Rat lymphocyte cultures with metabolic activation received S-9 homogenate prepared from male Sprague Dawley rats treated with Arochlor 1254; the final concentration of S-9 in culture was 2%. Replicate cultures were used for each test article concentration as well as for positive and control cultures. After 4 hours, cells were washed with medium and then placed in was tissue culture flasks containing buffered medium supplemented with 10% fetal bovine serum. Cultures were harvested 20 hours after termination of treatment. Approximately 3 hours prior to harvest, colcemid was added to each culture at a final concentration of 0.2 ug/ml.
Experiment 2: Approximately 48 hours after initiation of cultures, n-butyl propionate was added directly to culture flasks and allowed to incubate for 24 hours at 37 degree C in the absence of metabolic activation. Positive and negative controls were run concurrently. Replicate cultures were used for each test article concentration as well as for positive and control cultures. After 24 hours cultures were harvested. Approximately

3 hours prior to harvest, colcemid was added to each culture at a final concentration of 0.2 ug/ml.
Harvested cells were swollen by hypotonic treatement, fixed with methanol:acetic acid, placed on glass slides, and stained with Giemsa. All slides were coded prior to evaluation. Mitotic indices were determined as the number of cells in metaphase among 1000 cells per replicate and expressed as percentages. One hundred metaphases for each test article and negative control culture for a total of 200 cells per treatment. For positive control cultures, 50 to 100 cells were examined for chromosomal abnormalities and polyploidy. Structural chromosomal abnormalities included chromatid and chromosome gaps, chromatid breaks and exchanges, chromosome breaks and exchanges, and miscellaneous abnormalities such as chromosomal disintigration and chromosomal pulverization. Those cells having five or more aberrations per cell were classified as cells with multiple aberrations.
At each dose level, data from replicates were pooled. A two-way contingency table was constructed to analyze the frequencies of aberrant cells. An overall Chi-square statistic, based on the table, was partitioned into components of interest. Statics were generated to test the two global hypothesis of: (1) no differences in average number of cells with aberrations among the dose groups, and (2) no linear trend of increasing number of cells with aberrations with increasing dose (Armitage, P. 1971. Statistical Methods in Medical Research. John Wiley & Sons, Inc., New York, NY). An ordinal metric (0, 1, 2,...) was used for the doses in the statistical evaluation. If either statistic was found to be significant at $\alpha = 0.05$ versus a one-sided increasing alternative, pairwise tests (i.e. control vs test article) were performed at each dose level and evaluated at at $\alpha = 0.05$ again for a one-sided alternative. Polypoid cells were analysed by the Fisher Exact probability test. The number of polyploid cells was pooled across replicates for the analysis and evaluated at at $\alpha = 0.05$. The data was analysed separately based on the presence or absence of S-9 and exposure time (4 or 24 hours).
A test chemical is considered positive if it induces a significant dose-related increase in the incidence of cells with chromosomal aberrations.

Year:	2003
GLP:	yes
Test substance:	n-butyl propionate, purity 99.92%
Results:	n-butyl propionate did not induce a significant increase in the incidence of cells with chromosomal abnormalities at any of the concentrations evaluated. Approximately 48 hours after initiation of whole blood cultures, rat lymphocytes were treated for 4 or 24 hours with n-butyl propionate at target concentrations up to 1300 ug/ml (10 mM).

There was minimal toxicity in cultures exposed to butyl propionate for 4 hours, with reductions in mitotic indices ranging from 0 to 20%. Toxicity was observed, however, in cultures treated for 24 hours as evidenced by mitotic index reductions in mitotic of 72 and 82% for the higher concentrations tested, 650 and 1300 ug/ml, respectively.
In the presence of S-9 metabolic activation, cultures showed moderate to no toxicity with reductions in mitotic index ranging from 0 to 31%.
In both tests, there were no significant increases in the incidence of cells with aberrations as compared to negative (DMSO) controls. The aberration frequency in negative controls was within the limits of the laboratory historical values. Positive control cultures had significantly higher incidences of aberrant cells than negative controls.

Reference: Linscombe, V.A., Jackson, K.M., and Schisler, M.R. 2003. Evaluation of n-butyl propionate in an in vitro chromosomal aberration assay utilizing rat lymphocytes (unpublished report). Laboratory Project Study ID 021133. The Dow Chemical Company, Midland, MI.

5.6 GENETIC TOXICITY IN VIVO

(a)

Preferred value	
Type:	
Remark:	No data
Reference:	

5.7 CARCINOGENICITY

No data

5.8 TOXICITY TO REPRODUCTION

(a)

Preferred value	reliability score = 1, valid without restrictions; guideline study
Species:	rat
Strain:	Sprague-Dawley
Sex:	male and female
Route of Admin:	inhalation
Exposure Period:	13 weeks
Freq. of Treatment:	daily, 5 days/week
Post Exposure Observation Period:	8 week recovery
Doses:	0, 250, 750, 1500 ppm
Control Group:	yes
NOEL:	for reproductive organ effects: 1500 ppm

LOEL:

Method: USEPA TSCA Health Effects Test Guidelines for Subchronic Exposure Inhalation Toxicity (40 CFR 54, Guideline 798.4900, May 16, 1989.
Groups of 15 male and 15 female Sprague-Dawley rats (approximately 7 weeks old, 222-255 g for males, 151-183 g for females) were assigned to 4 groups and exposed to n-butyl propionate at target concentrations of 0, 250, 750, or 1500 ppm for 6 hours per day, 5 days per week, for 13 consecutive weeks for a minimum of 65 total exposures. Following 13 weeks of exposure, 5 rats per sex per group were arbitrarily selected for an approximate 8-week (non-exposure) recovery period.
Rats were housed individually in wire-mesh cages. All animals were housed separately by test group. During exposures, animals were housed in stainless steel wire-mesh cages; food and water was withheld during exposure. Animals were exposed in four 1-cubic meter glass and stainless steel whole-body inhalation chambers operated under dynamic conditions with airflows of at least 12-15 changes per hour, ensuring a minimum oxygen content of 19%. One chamber was designated for each exposure group. The control group was exposed to clean, filtered air under conditions identical to the test groups. All rats were exposed simultaneously in the four exposure chambers at approximately the same time each day. Chamber temperature and humidity was monitored continuously and recorded every 35 minutes.
Measured daily mean temperatures ranged from 22 degree C to 28 degree C (71 to 82 degree F) and daily mean relative humidity ranged from 34 % to 63%. Animals were rotated on a daily bases through various cage positions to compensate for possible variations in exposure concentrations. Vapor was generated by metering the liquid n-butyl propionate from a piston pump onto 8- and 12- mm glass beads within a glass vaporization column wrapped with flexible electric heating tape. Vaporization temperature was controlled by a model CN370 digital temperature controller (Omega Engineering).
Compressed air for vaporization was metered into the vaporization column below the glass beads. The vapor was piped to the chamber inlet where the concentration was reduced to desired levels by mixing with chamber ventilation air. Actual chamber concentrations were analyzed at approximate 35 minute intervals during exposure using a HP 5890 Series II gas chromatograph equipped with a flame ionization detector. Average measured chamber concentrations were within 1 to 2% of the target concentrations. All rats were observed twice daily for morbidity and mortality. A clinical examination was performed on all animals prior to each exposure. Animals were observed for clinical signs during exposure and approximately one hour after completion of exposure. On non-exposure days,

including the recovery period, clinical examinations were performed each day. Detailed physical examinations were conducted weekly, beginning one week prior to initiation of exposure, and just prior to scheduled sacrifice. Body weights of all animals were recorded weekly, beginning one week prior to exposure, and just prior to sacrifice. Mean body weights and body weight changes were calculated for each interval. Individual food consumption was recorded weekly for all animals, beginning one week prior to exposure. Blood samples from a lateral tail was collected for clinical pathology evaluations from all animals during study week 4 and from all animals designated for study week 13 necropsy; blood was collected from the vena cava during sacrifice by exsanguination. Gross examinations were performed and all major organs and tissues. Male reproductive tissues were examined grossly and collected for microscopic examination including the testes with epididymides, seminal vesicles, and prostate. Female reproductive tissues were examined grossly and collected for microscopic examination including the ovaries with oviducts and the uterus with vagina. Mammary gland tissue was also collected from females. The ovaries (females only), and testes (males only) from all animals were weighed. Microscopic tissue evaluations were performed on all tissues, including reproductive tissues, from animals in the control and 1500 ppm group.

Year: 1997

GLP: yes

Test substance: n-butyl propionate, purity 99.61%

Remark: Repeated exposure to n-butyl propionate at concentrations up to 1500 ppm produced few adverse effects to young adult male and female rats. No reproductive organ effects were noted and no effect on female mammary tissues were observed. The only systemic effects detected were reductions relative to controls in body weights, body weight gains, and feed consumption rates. These effects were found to be reversible, and normal values for these parameters were achieved after exposure had ceased. The most pronounced effect associated with exposure to n-butyl propionate vapor was an apparent local degenerative effect to the olfactory epithelium in the nasal epithelium . The NOEL for n-butyl propionate for reproductive organ effects is 1500 ppm.

Results: There was one male in the 250 ppm group found dead on exposure Day 41; necropsy revealed the cause of death was marked upper and lower urinary tract infection which was not considered to be test article-related. All other animals survived to scheduled necropsy. No exposure-related clinical signs were observed in during exposure or recovery periods. Other findings were seen infrequently in single animals and at similar incidences in control and treated groups. Mean body weight and

body weight gains in the 1500 ppm males were reduced by 10% and 20%, respectively, when compared to control males. During the recovery period, mean body weights and body weight gains were similar to control values; by the end of the recovery period, mean body weight in the 1500 ppm males was within 1% of the control group value. The 1500 ppm group females experienced slight, transient decreases in mean body weight during study weeks 0-1 and 2-3; no other adverse effects were observed on body weight data in the 1500 ppm female group. No body weight trends were apparent in the 250 and 750 ppm groups. Weekly food consumption was reduced for males in the 1500 ppm group throughout the exposure period; consumption was decreased by 15% when compared to controls at study week 12-13. Food consumption for 1500 ppm recovery group males was similar to control group values during the recovery interval. There were no exposure-related effects on food consumption in the 1500 ppm females or the 250 ppm and 750 ppm male or female rats. No consistent pattern of exposure-related changes were observed for hematology or clinical chemistry parameters. At necropsy, there were some differences noted for organ weights when compared to controls. At study week 13, 1500 ppm males displayed increased mean testes weights relative to final body weight. This change was considered secondary to the reduced final body weight mean in this group. Among recovery group males sacrificed after 8 weeks, no differences in testes weights were observed relative to controls. There were no macroscopic changes observed at necropsy that could be ascribed to n-butyl propionate exposure. There were no microscopic changes observed in any of the reproductive tissues from males or females in the 1500 ppm exposure groups. The only exposure-related findings were limited to the degenerative changes of the olfactory epithelium in the nasal cavity of rats in the 750 ppm and 1500 ppm groups.

Comment: The only deficiency of this study is that maternal toxicity was not evident at the highest dose tested.

Reference: 1) Ulrich, C.E. 1997. A 13-Week Inhalation Toxicity Study of n-Butyl Propionate in Albino Rats. WIL Research Laboratories, Inc., Ashland, OH. Unpublished study dated April 28, 1997.
2) Banton, M.I. et al. 2000. Subchronic and developmental toxicity studies of n-butyl propionate vapor in rats. J. Toxicol. Environ. Health 61: 79-105.

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

(a) Preferred value: reliability score = 1, valid without restriction; guideline study
Species: rat
Strain: Sprague-Dawley
Sex: female

Route of Admin:	inhalation
Exposure Period	gestational days (gd) 6 through 15
Freq. of Treatment:	6 hours/day for 10 consecutive days
Duration of Test	dams sacrificed on gd 21
Doses:	0, 500, 1000, or 2000 ppm
Control Group:	yes
LOEL (Maternal Toxicity):	500 ppm
NOEL (Teratogenicity):	≥2000 ppm
Method:	USEPA TSCA Toxicity Test Guidelines for Developmental Toxicity Studies (40 CFR, Vol 50, No 188, Guideline No. 798.4900), September 27, 1985).

Female Sprague-Dawley rats (approximately 12 weeks old, minimum weight 220 g) were paired with resident male breeding rats (1:1 ratio) and observed daily for evidence of breeding activity. Females positive for copulatory plug or vaginal smear were considered to be at day 0 of gestation. Mated females were randomly assigned to one of four groups, each containing 24 pregnant female Sprague-Dawley rats. Groups were exposed to n-butyl propionate vapor at concentrations of 500, 1000 or 2000 ppm for 6 hours/day on gestational days 6 through 15. Females were not exposed on gestation days 16-20. All rats were observed twice daily for mortality and morbidity. Detailed clinical observations were recorded individually from gestation day 0 through 20. Rats were housed in stainless steel wire-mesh cages. All rats were housed separately by test group. Animals were housed in an environmentally controlled room. Room temperature and humidity were recorded daily. Temperatures ranged from 21 to 23 degree C (70 to 73 degree F); humidity ranged from 34 % to 58%. During exposures, animals were housed individually, separated by test group, in stainless steel wire-mesh cages. Food and water was withheld during exposure but available *ad libitum* at all other times. Animals were exposed in four 1-cubic meter glass and stainless steel whole-body inhalation chambers operated under dynamic conditions with airflows of at least 12-15 changes per hour, ensuring a minimum oxygen content of 19%. One chamber was designated for each exposure group. The control group was exposed to clean, filtered air under conditions identical to the test groups. Chamber temperature and humidity was monitored continuously and recorded every 35 minutes. Measured daily mean temperatures ranged from 22 to 28 degree C (71 to 82 degree F) and daily mean relative humidity ranged from 34 % to 63%. Animals were rotated on a daily bases through various cage positions to compensate for possible variations in exposure concentrations.

Vapor was generated by metering the liquid n-butyl propionate from a piston pump onto 8- and 12- mm glass beads within a glass vaporization column wrapped with flexible electric heating

tape. Vaporization temperature was controlled by a model CN370 digital temperature controller (Omega Engineering). Compressed air for vaporization was metered into the vaporization column below the glass beads. The vapor was piped to the chamber inlet where the concentration was reduced to desired levels by mixing with chamber ventilation air. Actual chamber concentrations were analyzed at approximate 35 minute intervals during exposure using a HP 5890 Series II gas chromatograph equipped with a flame ionization detector. Average measured chamber concentrations were within 1 to 2% of the target concentrations.

A clinical examination was performed on all animals prior to each exposure. General observations of clinical signs were made for each group during the exposure period and for individual animals approximately 1 hour following completion of the exposure period. Individual maternal body weights were recorded on gestation days 0; maternal weights were recorded daily on gestation days 6 through 16, and on gestation day 20 prior to sacrifice. A groups mean body weight was calculated for each of these days and mean body weight changes were calculated for each interval as well as for gestation days 6-9, 9-12, 12-16, 16-20, and 0-20. Individual maternal food consumption was recorded on the corresponding gestation body weight days.

All dams were sacrificed on gestation day 20 and necropsies performed. A gross examination of all organs in the thoracic, abdominal, and pelvic cavities was conducted and the uterus and ovaries excised for further evaluation. The gravid uterine weight was recorded, as was the number of corpora lutea per ovary. The uterine contents were then examined, including the number and location of all live and dead fetuses, early and late resorptions, and the total number of implantation sites. Uteri with no macroscopic evidence of implantation were removed, opened and placed in an ammonium sulfide solution for detection of early implantation loss as described by Salewski (Salewski, V.I. 1964. Arch. Exp. Pathol. Pharmakol: 247: 367). Live fetuses were dissected from the uterus, counted, weighed, sexed and examined for external abnormalities. A visceral examination was also performed on all fetuses using a modification of the fresh dissection technique of Stuckhardt and Poppe which included the heart and major vessels (Stuckhardt, J.L. and Poppe, S.M. 1984. Teratogen. Carcinogen. Mutagen. 4: 181-188). For late resorptions, the crown-rump length and degree of autolysis were recorded and the tissue discarded. After gross examination, for approximately half the fetuses in each litter, the heads were removed, placed in Bouin's fixative, and processed for subsequent soft-tissue examination. The heads from the remaining fetuses were examined by a mid-coronal slice. All

	carcasses were then eviscerated, fixed in 100% ethanol, and processed for skeletal examination. External, visceral, and skeletal findings were recorded as developmental variations or malformations.
Year:	1997
GLP:	yes
Test substance:	n-butyl propionate, purity 99.1%
Remark:	Maternal exposure during organogenesis (gestation day 6-15) to up to 2000 ppm n-butyl propionate vapor did not produce marked effects on reproductive parameters or fetal development. The NOEL for developmental toxicity is $\geq$ 2000 ppm. Maternal toxicity, as evidenced by dose-related effects on maternal body weight and food consumption during exposure, was noted in all groups exposed to n-butyl propionate. The lowest concentration tested, 500 ppm, produced adverse effects. The LOEL for maternal toxicity is 500 ppm.
Result:	The predominant clinical signs observed during exposure were dose-related incidences of slightly drooping eyelids and salivation in the 1000 and 2000 ppm groups. At the 1-hour post-exposure examination, wet tan or yellow matting on various body surfaces was noted primarily in the 2000 ppm group. Exposure of timed-pregnant rats to n-butyl propionate vapor at concentrations of 500, 1000, and 2000 ppm during organogenesis resulted in maternal toxicity (see next section for description). At scheduled necropsy there were no treatment-related macroscopic findings in maternal animals. The mean gravid uterine weight was not affected by exposure to n-butyl propionate.
Maternal toxicity:	Exposure related effects on body weight and food consumption were observed in all exposed groups. The effect of n-butyl propionate on body weight occurred primarily during the early post-implantation organogenesis period (gestational days 6-9). Females adapted to exposure as reflected by improved body weight gain for the rest of organogenesis, even when food consumption was decreased. Food consumption was decreased in a dose-dependent manner in all exposure groups during the exposure period (gestation day 6-16). During the post-treatment period (gestation day 16-20, food consumption was similar to the control group.
Pregnancy/litter data:	Reproductive and fetal development parameters were not affected by exposure. There were no fetal deaths observed in any group. Analysis of fetuses revealed no treatment-related changes in the incidence of external, visceral, skeletal, or total malformations or variations. No dams aborted, delivered early, or were removed from study.
Fetal data:	Analysis of fetuses revealed no treatment-related changes in the incidence of external, visceral, skeletal, or total malformations or variations. The number of fetuses (litters) with malformations were 2 (2), 0 (0), 4 (4), and 1 (1) in the 0, 500, 1000, and 2000

ppm groups, respectively. Variations were limited to the skeleton and were observed in all exposure groups. All treatment groups exhibited increases in the incidence of reduced ossification of the 13th rib; however, the incidences expressed as percent per litter (3.2, 6.6, and 5.1% per litter in the 500, 1000, and 2000 ppm groups, respectively) were well within the range in the laboratory's historical control data (0.0 to 11.5%) and no dose-response was apparent. There was an increase in the number of litters in the 1000 ppm group with unossified sternebra(e) number 5 and/or number 6. Because the incidence (3.7% per litter) was well within the range of historical control data (0.6 to 37.5%), and because a similar increase was not observed in the 2000 ppm group, the difference was attributed to biological variation. Other skeletal variations observed in the treated group occurred infrequently and/or at similar frequencies in the control group.

Reference: 1) Nemec, M.D. 1997. An Inhalational Developmental Toxicity Study of n-Butyl Propionate in rats. WIL Research Laboratories, Inc., Ashland, OH. Unpublished study dated January 22, 1997. 2) Banton, M.I. et al. 2000. Subchronic and developmental toxicity studies of n-butyl propionate vapor in rats. J. Toxcicol. Environ. Health 61: 79-105.

(b)

Species:	rat
Strain:	Sprague-Dawley
Sex:	female
Route of Admin:	inhalation
Exposure Period:	gestation day 6-15
Freq. of Treatment:	6 h/day
Post Exposure	gestation day 16-20
Observation Period:	none
Doses:	0, 250, 500, 2500, or 4000 ppm
Control Group:	yes
NOEL (maternal toxicity):	500 ppm
NOEL (intrauterine survival):	4000 ppm

Method: Female Sprague-Dawley rats (approximately 12 weeks old, minimum weight 220 g) were paired with resident male breeding rats (1:1 ratio) and observed daily for evidence of breeding activity. Females positive for copulatory plug or vaginal smear were considered to be at day 0 of gestation. Mated females were randomly assigned to one of five groups, each containing 12 pregnant female Sprague-Dawley rats. Groups were exposed to n-butyl propionate at target concentrations of 0, 250, 500, 2500, or 4000 ppm for 2 weeks, 6 hours per day, 5 days per week, for two consecutive weeks for a total of 10 exposures. Rats were housed individually in wire-mesh cages. All animals were housed separately by test group. During exposures, animals were housed in stainless steel wire-mesh cages; food and water was withheld during exposure. Animals were exposed in five 1 cubic

meter glass and stainless steel whole-body inhalation chambers operated under dynamic conditions with airflows of at least 12-15 changes per hour, ensuring a minimum oxygen content of 19%. One chamber was designated for each exposure group. The control group was exposed to clean, filtered air under conditions identical to the test groups. All rats were exposed at approximately the same time each day. Chamber temperature and humidity was monitored continuously and recorded every 35 minutes. Measured daily mean temperatures ranged from 20 to 24 degree C (68 to 75 degree F) and daily mean relative humidity ranged from 23 % to 47%. Animals were rotated on a daily bases through various cage positions to compensate for possible variations in exposure concentrations. n-Butyl propionate vapor was generated by metering the liquid material from a piston pump onto 8- and 12- mm glass beads within a glass vaporization column wrapped with a flexible electric heating tape. Vaporization temperature was controlled by a model CN370 digital temperature controller (Omega Engineering). Compressed air for vaporization was metered into the vaporization column below the glass beads. The vapor was piped to the chamber inlet where the concentration was reduced to desired levels by mixing with chamber ventilation air. Actual chamber concentrations were analyzed at approximate 35 minute intervals during exposure using a HP 5890 Series II gas chromatograph equipped with a flame ionization detector. Average measured chamber concentrations were within 2 to 5% of the target concentrations. All rats were observed twice daily for morbidity and mortality. Animals were observed for clinical signs during exposure and approximately one hour after completion of exposure. Individual maternal body weights were recorded for gestation days 0, 6-16 (daily), and 20. A groups mean body weight was calculated for each of these days and mean body weight changes were calculated for each interval as well as for gestation days 6-9, 9-12, 12-16, 16-20, and 0-20 Individual maternal food consumption was recorded on the corresponding gestation body weight days.
All dams were sacrificed on gestation day 20 and necropsies performed. A gross examination of all organs in the thoracic, abdominal, and pelvic cavities was conducted and the uterus and ovaries excised for further evaluation. The gravid uterine weight was recorded, as was the number of corpora lutea per ovary. The uterine contents were then examined, including the number and location of all live and dead fetuses, early and late resporptions, and the total number of implantation sites.

Year:	1996
GLP:	yes
Test substance:	n-butyl propionate, purity 99.1%

Results:	There were no mortalities in any group. Exposure-related clinical signs observed in dams in the 2500 and 4000 ppm groups included drooping or half-closed eyelids and salivation during exposure, and dried brown or red material or staining around the mouth and/or nose, noted after exposure during daily examinations. An increased incidences of yellow or tan staining in the urogenital or ventral body surfaces was noted in the 4000 ppm group one hour following exposure. Reductions in mean body weight gains were noted during gestation days 6-16 in the 2500 and 4000 ppm groups. Mean body weight gains were similar to the control group during the post-treatment period (gestation day 16-20). Mean body weights in dams in the 2500 and 4000 ppm groups were reduced relative to control values during gestation days 7-16, and 20. Mean gravid uterine weights, net body weights, and net body weight gains were reduced in the 2500 and 4000 ppm groups. Exposure to n-butyl propionate had no effect on body weight data in the 250 and 500 ppm groups. Maternal food consumption was reduced in the 2500 and 4000 ppm groups during the entire treatment period (gestation days 6-16). Food consumption was comparable to controls during the post-treatment interval (gestation day 16-20). Food consumption was not affected by exposure in the 250 and 500 ppm groups. No exposure-related internal findings were observed at scheduled necropsy. Intrauterine survival was not affected by exposure to n-butyl propionate in the 250, 500, 2500, and 4000 ppm groups. Parameters such as postimplantation loss, live litter size, and numbers of corpora lutea and implantation sites were comparable to control values.
Reliability:	score = 1, valid without restriction; comparable to guideline study
Reference:	Nemec, M.D. 1996. A Combined 2-Week Range-Finding Inhalation Toxicity and Developmental Toxicity Study of n-Butyl Propionate in Rats. WIL Research Laboratories, Inc., Ashland, OH. Unpublished study dated November 14, 1996.

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

(a)

Type:	Neurobehavioral effects of repeated exposure
Species:	rat
Strain:	Fischer 344
Sex:	male and female
Route of Admin:	inhalation
Exposure Period:	11 days
Freq. of Treatment:	6 hours/day, 5 days a week for a total of 9 exposures
Post Exposure Observation Period:	26 days

Doses:	0, 800, 2600, 3200 ppm
Control Group:	yes
NOAEL:	3200 ppm for neurotoxic effects
LOEL:	
Method:	Equivalent to OECD 413

Male and female 344 rats were assigned to 4 groups, 10 per sex per group, and exposed to n-butyl propionate at target concentrations of 0, 800, 2600, 3200 ppm for 6 hours per day, 5 days per week, for a total of 9 exposures. An additional 10 animals per sex were included in the control and high dose (3200 ppm) groups. After the final exposure, 10 rats per sex from each group were sacrificed; the remaining animals in the control and high 3200 ppm groups (recovery group, 10 rats per sex per group) were held for a 26-day observation period and then sacrificed. Rats were approximately 55 days old at initiation of exposure. Animals were housed individually stainless steel wire-mesh cages. All rats were housed separately by test group. Food and water was withheld during exposure but available *ad libitum* at all other times. Animals were exposed in 1330 L stainless steel and glass inhalation chambers for 6 hours per day. Metering of the liquid n-butyl propionate into a heat glass evaporator generated vapours of the test material. Chamber concentrations were analysed approximately twice per hour by a gas chromatograph equipped with a flame ionization detector. Average chamber concentrations were within 1 to 3% of the target concentration. Chamber temperature and humidity were monitored continuously and recorded twice per hour during exposure. Daily mean chamber values ranged from 20.2 to 24.1 degree C; daily mean chamber relative humidity ranged from 29.6 to 59.1%. During exposures, clinical observations were recorded on a group basis. Preceding and following exposures, all animals were individually observed for signs of toxicity. On non-exposure days, animals were observed once per day for overt clinical signs and twice per day for morbidity and mortality. Ophthalmic examinations were conducted prior to first exposure, and following the last exposure. Body weights of all animals were recorded prior to exposure, and on Study Days 2,5,8,9 and immediately prior to sacrifice. Body weights for animals held during the post-exposure recovery period were recorded weekly and just prior to sacrifice. Serum chemistry and haematological evaluations were performed on blood samples collected from all rats on the day of sacrifice.
Prior to the first exposure, all animals were evaluated using a functional observational battery (FOB) of screening tests designed to detect alterations in central and peripheral nervous system function. During the second week of exposure, the FOB was performed again on all animals on Thursday (males only) and Friday (females only). The FOB testing regimen was

staggered over two days to accommodate the inhalation exposure schedule. During examination, each animal was placed on a clean laboratory cart covered with a think disposal paper board. The surface of the cart was surrounded by clear Plexiglas walls. The animal was observed for singns of convulsions, tremors, excessive vocalization, piloerection, and unusual behavior. Gait, body position, breathing pattern, arousal, defecation, urination, and rearing behavior was also evaluated. Approach, startle, and tail pinch responses were then evaluated. The animal was then grasped and muscle tone, lacrimation, salivation, and air righting reflexes were assessed. Animals were tested by trained technicians who were not aware of the animals' treatment.

Ten rats per sex per exposure group were individually housed in round polycarbonate metabolism cages; food and water consumption was measured for approximately 15 hours following 9 (females) or 8 (males) exposures. Urine was collected while rats were housed in metabolism cages, food and water was available *ad libitum*. Food and water consumption was measured, and urine was collected in a similar manner over a 16-hour interval for all recovery groups rats at the end of the 26-day recovery interval. Upon sacrifice, non-fasted animals were weighed, anaesthetised, and sacrificed by brachial artery exsanguination. A complete necropsy was performed on all animals.

Year: 1993

GLP: yes

Test substance: n-butyl propionate, purity 99.9%

Remarks: Four groups of 10 male and 10 female Fischer 344 rats were exposed to n-butyl propionate vapour at target concentrations of 0, 800, 2600, and 3200 ppm for 6 hours per day, 5 days per week, for a total of 9 exposures. During exposure, animals were observed for overt signs of reaction to treatment. Prior to the first exposure, all animals were evaluated using a functional observational battery (FOB) of screening tests designed to detect alterations in central and peripheral nervous system function. During the second week of exposure, the FOB was performed again on all animals on Thursday (males only) and Friday (females only). The FOB testing regimen was staggered over two days to accommodate the inhalation exposure schedule. Animals were tested by trained technicians who were not aware of the animals' treatment. No mortality occurred and there were no clinical signs of toxicity. Decreases in body weights or body weight gains were observed in males and females in all exposure groups. Exposure-related decreases in food consumption was observed for male and female rats in the 1600 and 3200 ppm groups, and decreases in water consumption was noted in females from the 1600 and 3200 ppm groups. There

	were no treatment related changes observed in the functional observational battery (FOB) evaluations. Under conditions of this assay, the NOEL for neurotoxicity was at least 3200 ppm.
Reliability:	score = 2, valid with restrictions
Remark:	A deficiency of this study is that brain and spinal chord tissue were not evaluated for neuropathology.
Reference:	Werley, M.S., Chun, J.S., and Kintigh, W.J. Union Carbide Corporation (unpublished report). n-Butyl Propionate: Nine-Day Vapor Inhalation Study in Rats. Bushy Run Research Center, Project ID 91U0091, May 7, 1993.

B. Toxicodynamics, toxicokinetics

No data available

C. Other

No data available

5.11 EXPERIENCE WITH HUMAN EXPOSURE

Remarks:	In human subjects, n-butyl propionate tested at 2% in petrolatum produced no irritation after a 48-hr closed-patch test.
Reference:	Epstein, W.L. 1978. Report to RIFM, 13 January 1978.

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